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, 2025

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, 2025 was approximately $3.4 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, 2026, the Company had 96,629,788 shares of common stock issued and outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement relating to its 2026 Annual Meeting of Stockholders, to be held on or about May 14, 2026, 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;
- our ability to address comments in the Complete Response Letter, or CRL, related to UX111 to the satisfaction of the U.S. Food and Drug Administration, or FDA, and the outcome of any resubmission of the Biologics License Application, or BLA;
- 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 in 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;
- our ability to achieve the anticipated savings from our recently announced restructuring plan;
- 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, government shutdowns, financial institution instability, changes in tariff policy, 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, outcomes 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 ultra-rare 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 ultra-rare genetic diseases with significant unmet medical need and clear biology.*** There are numerous rare and ultra-rare genetic diseases that currently have no drug therapy approved that treat the underlying disease. Patients suffering from these diseases often have a significant morbidity and/or mortality. We focus on developing and commercializing therapies for multiple such indications with the utmost urgency. We also focus on diseases that have biology that is well understood. We believe that developing drugs that directly impact known disease pathways will increase the probability of success of our development programs. Our modalities of biologics, small molecules, 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, Türkiye, 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.

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 (apazunersen)	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.

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, Mexico, 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

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 January 2026, we resubmitted our BLA seeking accelerated approval for UX111 (rebisufligene etisparvovec) as a treatment for patients with Sanfilippo syndrome Type A (MPS IIIA) to the FDA. The submission included substantial longer-term data on multiple measures of neurologic benefit to support an intermediate clinical endpoint for accelerated approval supported further by CSF heparan sulfate and other biomarker data, as agreed with the FDA during the last clinical review.

In February 2026, we received an Incomplete Response Letter, or IRL, from the FDA regarding our resubmitted BLA. The IRL requested additional supportive documentation related to our CMC responses to the CRL we received in July 2025. We plan to provide the requested documentation in a resubmission of the BLA.

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 September 2025, we announced longer term Phase 3 data from the 48-week crossover period that demonstrated patients showed an even greater reduction in mean daily cornstarch intake, compared to the initial 48-week treatment period. In the crossover period, the DTX401 group (n=20) had a mean reduction in daily cornstarch intake of 61% at week 96 compared to baseline and the crossover group (n=19) had a mean reduction in daily cornstarch intake of 61% at week 96 compared to week 48. At the end of the crossover period, the DTX401 group saw a reduction in mean nighttime cornstarch of 70% compared to baseline and the crossover group saw a mean reduction of 75% compared to week 48. Two-thirds of participants across both groups eliminated at least one nighttime cornstarch dose following treatment with DTX401. At week 96, 83% (10 out of 12 patients) of the DTX401 group and 95% (18 out of 19 patients) of the crossover group reported "minimally improved" to "much improved" changes in disease burden as measured by the Patient Global Impression of Change (PGIC), a single item questionnaire that asked participants how their condition changed since the start of the study.

As of the data cut-off, glycemic control was maintained in participants treated with DTX401 despite significant reductions in daily cornstarch intake. DTX401 has demonstrated a consistent and acceptable safety profile with no new safety signals identified as of the data cut-off.

These results have been included in a rolling BLA submission that began in August 2025 and was completed in December 2025. The company expects a PDUFA action date in the third quarter 2026, based on FDA regulations.

GTX-102 (apazunersen) 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 Breakthrough Therapy Designation, 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 July 2025, we announced that all patients in the 48-week Phase 3 *Aspire* study have been enrolled. In total, 129 patients, between four and 17 years of age, with a genetically confirmed diagnosis of full maternal UBE3A gene deletion were enrolled and randomized 1:1 to the GTX-102 or the sham comparator group. Data from this study are expected in the second half of 2026.

In October 2025, we announced enrollment had begun in the Phase 2/3 *Aurora* study, which evaluates GTX-102 in other Angelman syndrome genotypes and ages.

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

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 *Enh3ance* 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 (i) the percentage of patients who achieve a response as measured by the change in 24-hour plasma ammonia levels and (ii) discontinuation or reduction ammonia-scavenger medications and protein-restricted diet. Based on the amended protocol, the change in 24-hour ammonia levels was measured through Week 36, after which the study unblinds 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 approximately 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 September 2025, we completed enrollment of five patients in Cohort 4 in the ongoing, 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 four, sequential dosing cohorts (Cohort 1; 5.0 x 10^12 GC/kg; Cohort 2: 1.0 x 10^13 GC/kg: Cohort 3; 2.0 x 10^13 GC/kg and Cohort 4; 4.0 x 10^13 GC/kg). Data from Stage 1 of this study are expected in 2026.

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

UX143 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. UX143 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 FDA and EMA Rare Pediatric Disease designation and Breakthrough Therapy Designation from the FDA, and was accepted into the EMA's Priority Medicines, or PRIME, program. UX143 is subject to our collaboration agreement with Mereo.

In December 2025, we announced that the Phase 3 *Orbit* and *Cosmic* studies did not achieve their primary endpoint of reduction in annualized clinical fracture rate compared to placebo (*Orbit*) or bisphosphonates (*Cosmic*).

In January 2026, topline safety and efficacy data from both studies were presented and included data on bone mineral density, vertebral fractures, and patient reported outcomes on pain and physical function. Additional analyses are ongoing to determine if there is a potential path forward for the program.

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

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 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 3 program from Ionis, ION582 an ASO, Oak Hill Bio, rugonersen an ASO, Neuren Pharmaceuticals, NNZ-2591 an IGF-1 analog, and MavriX Bio, a gene therapy.

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 (acquired by KKC) 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, JR-441, in Phase 1/2 by JCR Pharma, and GC1130A/NP3011, in Phase 1 by GC Biopharma/Novel Pharma.

With respect to DTX401, there are currently no pharmacologic treatments for patients with GSDIa. We are aware of a gene editing program specifically for R83C variants, BEAM-301, in Phase 1/2 by Beam Therapeutics, and 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, iECURE, ECUR-506 a gene editor, and Camp 4, CMP-001 an ASO.

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, and a gene therapy LY-M003, in Phase 1 by LingYiMed.

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, AGA2115, a bispecific sclerostin & DKK-1 antibody in Phase 2 by Angitia Bio, and a mesenchymal stem cell program in Phase 1/2 by Boost Pharma.

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. Potential obligations under these agreements are further described in "Note 8. License and Research Agreements" to the Consolidated Financial Statements.

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 Türkiye.

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. 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 Türkiye. In Türkiye, 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 based on net sales. We also pay KKC a 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 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 revenue share 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 and November 2025, we sold to OCM LS23 Holdings LP, an investment vehicle for the Ontario Municipal Employees Retirement System, or OMERS, a percentage of the future royalty payments based on net sales of Crysvita in the U.S. and Canada, subject to caps, with payments beginning in April 2023 and January 2028, respectively.

KKC pays us a royalty based on net sales in the European Territory. We subsequently sold this interest 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, Türkiye, 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 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 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 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 entered into a collaboration agreement with Regeneron to commercialize Evkeeza for HoFH outside the U.S. Under the agreement, we received rights to develop, commercialize, and distribute the product for HoFH in countries outside the U.S. Regeneron supplies the product and charges a product purchase price.

We are obligated to pay for certain future 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.

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, royalties 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. This license agreement was terminated for certain indications in November 2025.

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. This option and license agreement was terminated in November 2025.

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 UPENN 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 if certain development milestones are achieved over time. We will also make milestone payments for product approvals, if certain commercial milestones are achieved, and will pay 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, as subsequently amended, or Option Agreement, to collaborate on the development of GeneTx's GTX-102, an ASO for the treatment of Angelman syndrome. In July 2022, we exercised our option to acquire GeneTx, pursuant to the terms of the Option Agreement. During the year ended December 31, 2024, we achieved a regulatory milestone upon the initiation of the Phase 3 *Aspire* clinical study for GTX-102. We are obligated to pay additional regulatory approval milestones for the achievement of U.S. and EU product approvals and commercial milestone payments based on annual worldwide net product sales, contingent upon the achievement of the milestones. We will also pay 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. We have recognized certain clinical milestones under the TAMU agreement, and have obligations for future milestones, if achieved, a nominal annual license fee, as well as royalties on 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., Türkiye, 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 an upfront payment to Mereo. We have recognized certain regulatory milestones and have future obligations for additional regulatory and sales milestones under the agreement, if achieved. We will pay for all global development costs as well as royalties to Mereo on net sales in the U.S., Türkiye, and the rest of the world, and Mereo will pay us a 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 for reimbursing 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 royalties on net sales and commercial milestone payments 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 development and regulatory milestones as well as royalties of net sales.

Patents and Proprietary Rights

The proprietary nature of, and protection for, our products, product candidates, processes, and know-how are important to our business. Our success depends in part on our ability to protect 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, 2025, we own, jointly own, or have exclusive rights to more than 300 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, 2025, we own, jointly own, or have exclusive rights to more than 300 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, 2025, are summarized below.

Product	Territory[1]	Exclusivity[2]	Expiration
Crysvita® (burosumab)	U.S.	Patent: Crysvita antibody and sequences	Apr 2032
		Patent: Methods of treating XLH and TIO	May 2035
		FDA biologics exclusivity	Apr 2030
		FDA orphan exclusivity for TIO	Jun 2027
Mepsevii® (vestronidase alfa)	U.S.	Patent: Mepsevii enzyme and methods of treating MPS VII	Mar 2035
		FDA biologics exclusivity	Nov 2029
Dojolvi® (triheptanoin)	U.S.	Patent: Triheptanoin compositions	Apr 2029
		Patent: Pharmaceutical-grade triheptanoin	Nov 2034
		FDA orphan exclusivity for LC-FAOD	Jun 2027
Evkeeza® (evinacumab)	Europe	Patent: Evkeeza antibody and sequences	Jun 2036[3]
		Patent: Methods of treating atherosclerosis	Feb 2037
		Patent: Methods of treating familial hypercholesterolemia	Apr 2037
		EMA marketing exclusivity	Jun 2031

[1] Unless otherwise indicated, the table reflects exclusivity positions in the U.S. Evkeeza is included on an ex-U.S. basis, as we only hold commercialization rights outside the U.S. The Company maintains patent and regulatory exclusivities in multiple jurisdictions worldwide.
[2] One or more patents with the same or earlier expiration dates may fall under the same general subject matter and are not listed separately.
[3] Expiration date following term extension provided by SPC in most European countries; this expiration date has additionally been extended by six months to Dec 2036 in certain European countries via a PIP extension.

DTX401 (pariglasgene brecaparvovec)

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)

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)

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)

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 (apazunersen)

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)

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 two issued U.S. patents expiring in 2039 (not accounting for any available PTE). Beyond this in-license, we own a patent family covering AAV vectors expressing a novel truncated version of the ATP7B protein produced by UX701; this patent family includes an issued U.S. patent expiring in 2042 (not accounting for any available PTE).

Trademarks

We own registered trademarks covering the Ultragenyx mark in the U.S. and multiple other jurisdictions. 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

Our manufacturing network is a combination of internal capabilities and external contract management and development organization, or CDMO, partners. We believe this hybrid approach optimizes our capital investments while leveraging mature CDMO networks depending on the technical modality. For our AAV gene therapy products, we have the capabilities to manufacture and test our own drug substance and drug products while also leveraging CDMO partners.

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. The drug product is manufactured by BSP Pharmaceuticals, our CDMO partner. 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. The drug product is manufactured by Patheon Pharma Services by ThermoFisher Scientific, our CDMO partner. The transfer of drug product manufacturing sites was completed during the fourth quarter 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 at our gene therapy manufacturing facility and by 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 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. Reimbursement from Medicare, Medicaid and other third-party payors may be subject to periodic adjustments as a result of legislative, regulatory and policy changes as well as budgetary pressures in the U.S. and globally. For example, the One Big Beautiful Bill Act of 2025, or OBBBA, enacted changes to Medicaid eligibility, cost-sharing, and financing that could result in relatively lower reimbursement due to decreased beneficiary enrollment and budgetary pressures.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state measures designed to, among other things, reduce the cost of prescription drugs, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, in May 2025, the Trump Administration renewed the idea of international reference pricing through an executive order entitled "Delivering Most-Favored-Nation Prescription Drug Pricing to American Patients", which, among other things, directs the U.S. Department of Health and Human Services, or HHS, and other agencies to communicate most-favored-nation, or MFN, price targets to pharmaceutical manufacturers to bring prices for U.S. patients in line with comparably developed nations and to facilitate direct-to-consumer purchasing programs.

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, 2025, 45% of our total revenues were generated by our collaboration partner KKC.

Human Capital

General Information

As of December 31, 2025, we had 1,371 total employees, of which 916 are in research and development and 455 are in sales, general, and administrative. Further, 1,144 employees are based in the U.S., including at our facilities in Novato, California, Brisbane, California, Somerville, Massachusetts, Bedford, Massachusetts, and Woburn, Massachusetts, and 227 employees are based at our international locations. The majority of new employees hired during the year ended December 31, 2025 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.

In February 2026, we initiated a strategic restructuring plan to significantly reduce expenses, which includes a 10% workforce reduction of approximately 130 employees across the company. We regularly evaluate our business needs and opportunities and balance 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.
- Our future financial performance depends on the successful commercialization of our products and product candidates.
- 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 if we do not achieve our projected development goals.
- We may experience difficulty in enrolling patients.
- The regulatory approval processes 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 are subject to regulatory scrutiny, even after 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 supply and commercialization of Crysvita in certain major markets.
- We rely on third parties to manufacture our products and product candidates.
- The failure to supply by any of our single-source suppliers 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 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 or from generic versions of our small-molecule products and product candidates.
- 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.
- Changes to patent laws in the U.S. and other jurisdictions could diminish the value of patents in general.
- 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.
- Changing regulatory standards may make it difficult to accurately predict the likelihood of obtaining marketing approval.
- We may fail to comply with laws and regulations or changes in laws and regulations could adversely affect our business.
- Increasing use of social media could give rise to additional liability;
- We are exposed to risks related to international expansion of our business outside of the U.S.

- 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.
- We may experience unexpected costs or not achieve our anticipated savings from our recently announced strategic restructuring plan.
- 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 additional tax liabilities related to our operations, our ability to use our net operating loss carryforwards, costs of litigation, stockholder activism and 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 in 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, our ability to obtain regulatory and marketing approval of our product candidates and within our anticipated timeframes, the success of our commercialization efforts, and the rate of our future expenditures. We anticipate that our expenses could increase if and as we, among other things:

- 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;
- 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;
- 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.

Our future financial performance depends on the successful commercialization of our products and product candidates.

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 establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate (in amount and quality) product supply to support market demand for our products;
- 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 collaboration, licensing, or other arrangements; and
- maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how.

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, 2025, our available cash, cash equivalents, and marketable securities were $737 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. See “Item 7. Management’s Discussion and Analysis of Financial Condition and Results Of Operations—Funding Requirements” for additional information on the factors affecting our funding requirements.

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, which are often impacted by changes in macroeconomic conditions, including changing interest rates, inflation and market instability arising from political and trade tensions (including government shutdowns). 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. 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. For example, in December 2025, we announced that our UX143 Phase 3 *Orbit* and *Cosmic* studies did not achieve their primary endpoints despite promising Phase 2 results, and as a result, we are implementing significant expense reductions. In addition, 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;
- 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 develop, obtain regulatory approval for, and commercialize our products. 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 future product candidates will ever obtain regulatory approval. Further, as the clinical trial requirements and criteria of regulatory authorities 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. For more information, see “Item 1. Business – Government Regulation” above.

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 in "Item 1. Business – Government Regulation" of this Annual Report. 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.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel, accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Changes in the leadership of the FDA and other federal agencies under the current administration, including return-to-office policy, hiring freeze, and other policies, may lead to changes in the operations of the FDA, which may have a material impact on the industry and our clinical development plans. There have been widespread layoffs across various governmental agencies, including at the FDA, and other employees, including senior leaders at certain agencies, have resigned in response to the reforms, the full impact of which is unclear at this time. In addition, there is uncertainty around the funding, functioning and policy priorities of various governmental agencies, including the FDA. Disruptions or changes in how the FDA operates due to these policies could result in delays in FDA review or approval of our product candidate applications. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Further, applications for our product candidates could fail to receive regulatory approval, or could be delayed in receiving regulatory approval, for several other reasons, including but not limited to the following:

- 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, 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;
- failure to comply with an agreed upon PIP which 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 such is within the discretion of the relevant regulatory agency. Accordingly, even if we believe one of our product candidates meets the criteria for one of these designations, 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, 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.

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 that reveal a high and unacceptable severity and prevalence of adverse side effects can lead to suspension or termination, 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. There are only 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, EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

In addition, the 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, the FDA, the EMA or other foreign regulatory authorities may require that we not distribute a lot until the agency authorizes its release. 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.

Our products are subject to regulatory scrutiny, even after approval.

Our product candidates are subject to regulatory scrutiny, and 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 inspection and continual review to assess compliance with GMP and adherence to commitments made in any NDA, BLA, MAA, or other comparable application for approval in another jurisdiction. With respect to our third-party contract manufacturers, although we are not involved in their day-to-day operations, 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 or be unable to pass a federal, national or international regulatory inspection. For instance, in July 2025, we received a CRL from the FDA for our BLA for UX111, which cited information and improvements related to the observations from the FDA's inspections at our gene therapy manufacturing facility and that of our third-party manufacturer. 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, denial of or delays to product approval, withdrawal of product approval, enforcement actions and

criminal or civil prosecution. If our supply, or supply from one of our approved manufacturers 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 to 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 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 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 products, and decreased demand for our products.

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. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review in jurisdictions in which we operate 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. 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 a given 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. Failure to comply with GLP, GMP, or GCP regulations may result in denial for 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, which can lead to, delays and materially impacting 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 Türkiye, 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 or regarding market access and pricing in countries where it has the sole right to commercialize the product candidates that limit or negatively impact our commercialization efforts in those countries or 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, which would adversely affect 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.

We rely on third parties to manufacture, store and distribute our products and product candidates and, 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 "- Our products are subject to regulatory scrutiny, even after approval." 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 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. 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 recently enacted BIOSECURE Act, which, among other things, prohibits U.S. federal funding in connection with biotechnology equipment or services produced or provided by certain designated "biotechnology companies of concern" as determined by the Office of Management and Budget, , 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.

We focus our research and product development on treatments for rare and ultra-rare genetic diseases. Given the small number of patients who have the diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with the rare and ultra-rare genetic diseases we are targeting. 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.

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.

As we increase the number and range of our commercialized products, particularly as we prepare for launches of our first gene therapy products, we will need to expand our commercial and support teams to include additional expertise in those products. We may also 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 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 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. For example, deteriorating economic conditions and political instability in certain Latin American countries and in Türkiye 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 HHS 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. Furthermore, the OBBBA effected changes to Medicaid eligibility, cost sharing and financing that could result in relatively lower reimbursement due to decreased beneficiary enrollment and budgetary pressures.

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. 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 instances can 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. We expect to experience pricing pressures in connection with the sale of any of our products 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 and actions by elected officials. In addition, in May 2025, the Trump Administration issued an executive order entitled “Delivering Most-Favored-Nation Prescription Drug Pricing to American Patients”, which, among other things, directs the HHS and other agencies to communicate most-favored-nation price, or MFN, targets to pharmaceutical manufacturers to bring prices for U.S. patients in line with comparably developed nations and to facilitate direct-to-consumer purchasing programs. The HHS subsequently issued guidance indicating the MFN target price will be the lowest price paid in an Organisation for Economic Co-operation and Development country with a gross domestic product, or GDP, per capita of at least 60% of the U.S. GDP per capital. CMS also announced plans to extend MFN pricing to state Medicaid programs in exchange for those programs adopting uniform coverage criteria. It is currently unclear whether and to what extent these measures will be implemented and what impact any such implementation would have on our business. Further, there can be no assurance that the current administration or future administrations will not pursue different or additional measures that could impact drug pricing in the U.S. 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 licensors 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 could increase the uncertainties and costs surrounding the prosecution of our patent applications and the maintenance, 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 provides our competitors with a new forum in which to seek central revocation of our European patents and allows 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 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 some of 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 may not be sufficient to protect our proprietary technology and processes. This increases 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 does not necessarily 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.

Furthermore, our efforts to assess our employees, consultants, and independent contractors and prevent their use of the proprietary information or know-how of others, including former employers, in their work for us may not be successful, and we may in the future be subject to claims that such persons have wrongfully used or disclosed confidential information of third parties. Any resulting litigation could lead to, among other things, paying monetary damages, the loss of intellectual property rights or personnel, or substantial costs and the distraction of management and other personnel, any of which could adversely impact our business.

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 certain methods that may be used in the manufacture or delivery of one or more of our gene therapy product candidates. 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 continues to evolve through ongoing FDA implementation and judicial interpretation. 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 which could adversely affect our business and financial results.

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, and UX701 product candidates. Some of these patents and patent applications are licensed 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 may infringe our patents or the patents of our licensors. If we or one of our licensing partners were to initiate legal proceedings against a third party to enforce a patent covering our products or one of our product candidates, the defendant could counterclaim that the patent covering our product or product candidate is invalid and/or unenforceable. For example, in September 2024, we filed a patent infringement suit under the Hatch-Waxman Act against Navinta, Aurobindo and Esjay. See "Item 3. 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.

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.

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 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. In July 2025, we received a CRL from the FDA for our BLA for UX111, which cited information and improvements related to the observations from the FDA's inspection at our gene therapy manufacturing facility that will need to be resolved with the FDA before approval of UX111. If we are unable to resolve the FDA's observations related to our manufacturing facility, approval for UX111 and potentially for our other gene therapy candidates manufactured at our facility would be further delayed or denied. The cGMP requirements govern quality control of the manufacturing process and documentation policies and procedures. Our efforts to comply with cGMP require that we 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. Further, our recent strategic restructuring plan and workforce reduction could lead to additional recruitment challenges as well as increase in turnover of key employees. The inability to recruit and retain qualified personnel, or the loss of the services of Dr. Kakkis or any of other member of our executive leadership team or other key employee, may impede the progress of our research, development, and commercialization objectives.

If we fail to obtain or maintain orphan drug exclusivity for our products, our competitors may sell products to treat the same conditions and our revenue will be reduced. 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. Additionally, there may be future healthcare reform measures that reduce the exclusivity protections provided to already approved biological products.

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

We have recorded on our Condensed 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, 2025.

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. 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;
- 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;
- the market for a product candidate may change during our program so that such a product may become unreasonable to continue to develop; 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 and, even if our resources are allocated properly, may not necessarily lead to 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.

Regulatory standards are subject to change over time, making it difficult to accurately predict the likelihood of marketing approval even when clinical trials meet their endpoints.

Regulatory standards are promulgated by various government entities and are subject to change based on factors such as scientific developments, public perceptions of risk, and political forces. Because clinical trials often take years to complete, it is sometimes possible for standards that exist during the conception and initiation of a clinical trial to change before the clinical trial is completed or reviewed by government regulators. For example, we may initiate clinical trials that are designed to show benefits on relatively short-term endpoints, but ultimately be required to show benefits in longer-term outcome studies. While some government entities have safeguards intended to ensure standards agreed upon by sponsors and regulators at the outset of a clinical trial are applied during regulatory review processes, those safeguards generally permit regulators to apply more rigorous standards where regulators believe doing so is necessary. As such, there can be no assurance that regulatory standards that are appropriate at the outset of a clinical trial program will not become more rigorous during the regulatory approval process and could potentially result in a delayed approval or denial of marketing authorization.

In addition, the FDA, EMA and other regulatory authorities may change their policies, issue additional regulations or revise existing regulations, or take other actions, which may prevent or delay approval of our future products under development on a timely basis. Such policy or regulatory changes could impose additional requirements upon us that could delay our ability to obtain approvals, increase the costs of compliance or restrict our ability to maintain any marketing authorizations we may have obtained. In June 2024, the Supreme Court overruled the Chevron doctrine, which had given deference to regulatory agencies' statutory interpretations of ambiguous regulations in litigation against federal government agencies, such as the FDA. The overruling of the Chevron doctrine may significantly increase the number of challenges brought by companies and other stakeholders against federal agencies such as the FDA and its longstanding decisions and policies, including the FDA's statutory interpretations of market exclusivities and the "substantial evidence" requirements for drug approvals, which could undermine the FDA's authority, lead to uncertainties in the industry, and disrupt the FDA's normal operations, any of which could delay the FDA's review of our regulatory submissions. We cannot predict the full impact of this decision, future judicial challenges brought against the FDA, or the nature or extent of government regulation that may arise from future legislation or administrative action.

In January 2025, an executive order entitled "Unleashing Prosperity Through Deregulation," was issued which calls for at least 10 existing regulations to be repealed whenever an executive department or agency publicly proposes for notice and comment or otherwise promulgates a new regulation. Recent developments at the FDA include announcement of a plan to phase out animal testing for monoclonal antibodies and certain other drugs, the proposed rare disease evidence principles (RDEP) program to facilitate approval of drugs to treat rare diseases with very small patient populations with significant unmet medical need and with a known genetic defect that is the major driver of the pathophysiology, and the announcement of a new Commissioner's National Priority Voucher program for companies supporting certain U.S. national health priorities and interests. To the extent our competitors are selected for this new voucher pilot program, or are otherwise able to participate in any of these initiatives intended to accelerate drug development and application review, and obtain faster approval than us, our competitive position may be harmed. The FDA has also increased its scrutiny of foreign drug manufacturing facilities and other contractors based in China, especially with respect to the transfer of biological materials, genetic data, and other sensitive data of American patients to parties located in China. It is unclear how our industry and our clinical programs will be impacted by policies and regulations implemented under the current administration and FDA leadership, or other executive orders. There is significant uncertainty in the industry and how federal agencies like the FDA will change in the coming years under the current administration. To the extent the agency reorganization and other agency changes lead to disruptions in the FDA's operations, our correspondence and regulatory review processes with the FDA may be materially delayed.

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, AI-related laws and regulations, and tax laws and regulations. In certain jurisdictions, these regulatory requirements may be more stringent than those in the U.S., and in other circumstances these requirements may be 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; patient and non-patient privacy laws and regulations, including the European General Data Protection Regulation (EU) 2016/679, or GDPR, in the EEA, the GDPR as incorporated into UK law pursuant to the European Union (Withdrawal) Act 2018, or the UK GDPR, in the UK, the 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, the California Consumer Privacy Act of 2018, or CCPA, as amended by the California Privacy Rights Act of 2020, or CPRA, and California's Confidentiality of Medical Information Act; and the evolving global landscape for AI-related laws and regulations, which may impose obligations on companies developing and using AI and include U.S. federal and state laws and regulations and the EU Artificial Intelligence Act, 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. 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 and UK GDPR impose a number of strict obligations and requirements for processing personal data of individuals (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), in particular with respect to special categories of personal data like health data which is subject to specific requirements. EU member states may also impose additional requirements in relation to the processing of personal data, including special categories of personal data through their national legislation. In addition, the GDPR and UK GDPR impose specific restrictions on the transfer of personal data to countries outside of the EEA or UK 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 the EEA and UK's standard contractual clauses) along with further requirements, in particular the conduct of transfer risk assessments to verify if anything in the law and/or practices of the third country may impinge on the effectiveness of the safeguards in the context of the transfer at stake and, if so, to identify and adopt supplementary measures.

In the US, there are also several compliance requirements under HIPAA/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, including due to employee or consultant fraud or other misconduct, 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.

Increasing use of social media could give rise to liability and result in harm to our business.

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 or the inadvertent disclosure of material, nonpublic information, cause reputational harm or result in public exposure of personal information of our employees, clinical trial patients, customers, and others. We may also encounter criticism on social media regarding our company, management, or medicines. Negative posts or comments about us or our products on social media could seriously damage our reputation, brand image and goodwill.

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. Changes in policy with respect to sanctions or tariffs, including tariffs imposed by the U.S. on imports from most countries, and related retaliatory tariffs on U.S. goods, could also increase our costs or adversely impact our revenues. For instance, the current Presidential Administration has imposed tariffs on pharmaceutical products from certain countries, such as those imposed in the U.S. and E.U. trade agreement announced in July 2025. In September 2025, the Administration announced that future tariffs of up to 100% could be implemented affecting branded or patented pharmaceutical products coming into the U.S., unless the importing company is building U.S. manufacturing capacity. It is not yet clear whether these tariffs would apply to the importation of active pharmaceutical ingredients and possibly bulk drug products that are intended for use in clinical trials and not for commercial sale, which could increase the costs of materials for our clinical trials. There can be no assurance that future tariffs, trade agreements or other governmental actions will not impact pharmaceutical products from other countries, include the active ingredients or materials used in such products, or impose tariffs at a higher level than contemplated in previously announced trade agreements, any of which could significantly and adversely impact our operations and revenue.

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;
- 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.

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. Among other requirements, 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 personal 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, and the use of AI by us or the third parties on which we depend to operate our business may create new cybersecurity vulnerabilities, including those which may not be recognized at this time. 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 on 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 on which we depend to operate our business, have experienced cybersecurity incidents, including 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 cyberattacks 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, other proprietary or confidential information or personal 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, unauthorized access, use or disclosure of trade secrets, other confidential or proprietary information, protected health information, or other personal information, unauthorized 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 may also require 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, 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 experience difficulties, delays or unexpected costs and not achieve anticipated benefits and savings from our recently initiated strategic restructuring plan.

In February 2026, we initiated a strategic restructuring plan, which includes a 10% workforce reduction of approximately 130 employees across the company. Our workforce reduction may cause disruptions to our business operations. For example, the workforce reduction has resulted in the loss of a number of long-term employees, the loss of institutional knowledge and expertise and the reallocation and combination of certain roles and responsibilities across the organization, all of which could adversely affect employee morale and our operations. In addition, we may not be able to achieve the anticipated benefits or effectively realize all the cost savings anticipated from the reduction in force and we may incur unanticipated charges or make additional cash payments as a result of such initiatives that were not previously contemplated which could result in an adverse effect on our business or results of operations.

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 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 shares of common stock of Solid Biosciences, Inc., or 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 a 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 such 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 or regarding market access in 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;
- 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;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- 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, inflation, and market instability arising from increasing political and trade tensions;
- 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, 2025, there were 7.9 million 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, 2025, there were 6.2 million shares available for issuance under the A&R ESPP.

Our board of directors has adopted an Employment Inducement Plan, which was subsequently amended, or the Inducement Plan. At December 31, 2025, there were 0.3 million 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

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. For example, the OBBBA permits the expensing of certain research and development expenditures in the U.S. incurred in tax years beginning in 2025, while amortization over fifteen years continues to be required for foreign-based expenditures. 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 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.

Scrutiny regarding ESG practices and disclosures, as well as existing and proposed laws and regulations related to these topics, could result in additional costs and adversely impact our business and reputation.

Certain institutional and individual investors have increasingly used environmental, social, and governance , or ESG, screening criteria when making investment decisions. Investors and other stakeholders' expectations and standards for ESG practices are varied and evolving, and may be inconsistent with our practices. It is not possible for our ESG reporting, initiatives, or practices to satisfy all stakeholders, who have varied and sometimes incompatible views on ESG matters, and our reputation, our ability to attract or retain employees or our attractiveness as an investment could be negatively impacted. Investors may seek to modify our current ESG disclosures and practices or implement policies that are costly or adverse to our business, and there can be no assurances they will not advocate, via proxy contests, media campaigns or other public or private means, for us to make certain changes or engage in certain corporate actions on these topics.

In addition, our pursuit of, or failure (actual or perceived) 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, in addition to reputational harm. 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. Further, as a recipient of government funding, we may also risk the loss or rescission of such funding, or be required to modify our ongoing research or business practices, to the extent federal or state procurement policies or priorities evolve, including as it relates to the consideration of diversity, environmental, or other ESG-related criteria or considerations.

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 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 an Executive Director of IT Infrastructure and Cybersecurity, 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 Executive Director of IT Infrastructure and Cybersecurity 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 Executive Director of IT Infrastructure and Cybersecurity has over 25 years of experience managing information technology and cybersecurity matters and is certified as a Certified Information Security Manager. 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 updates on cybersecurity and information technology matters and related risk exposures from our CIO on at least an annual basis. 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 table below. 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 2031
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

In September 2024, we filed a patent infringement suit under the Hatch-Waxman Act against Navinta LLC, or Navinta, Aurobindo Pharma Limited, or Aurobindo, and Esjay Pharma LLC, or 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 Abbreviated New Drug Applications, or ANDAs, with the FDA, seeking FDA approval to market a generic version of Dojolvi® (triheptanoin). 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, in February 2026, a patent relating to certain pharmaceutical compositions of triheptanoin, including Dojolvi, issued in the United States and is expected to expire in 2034. We expect to list this patent in the Orange Book shortly. Dojolvi is also protected in the U.S. by orphan drug exclusivity for the treatment of pediatric and adult patients with molecularly confirmed long-chain fatty acid oxidation disorders (LC-FAOD) until 2027.

In December 2024, Esjay filed a motion to dismiss the suit and in April 2025, Navinta filed a motion for judgment on the pleadings, which we opposed in May 2025. Discovery is ongoing.

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

In October 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.

In February 2025, we filed an amended complaint following Catalent's response and Catalent subsequently moved to dismiss the amended complaint. In December 2025, the court denied Catalent's motion to dismiss our fraud claim. In January 2026, Catalent answered our complaint and filed a counterclaim against us for breach of contract related to disputed invoices, seeking damages of approximately $8 million plus interest.

Steven Bailey v. Ultragenyx Pharmaceutical Inc., Emil D. Kakkis, and Eric Crombez, M.D.

In February 2026, Steven Bailey filed a putative class action on behalf of certain of our stockholders against the Company, our CEO and our Chief Medical Officer in the United States District Court for the Northern District of California. The complaint asserts claims under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended, alleging that the Company made false and misleading statements about the design and prospects of the UX143 *Orbit* and *Cosmic* clinical trials. The lawsuit seeks unspecified damages and other relief.

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.

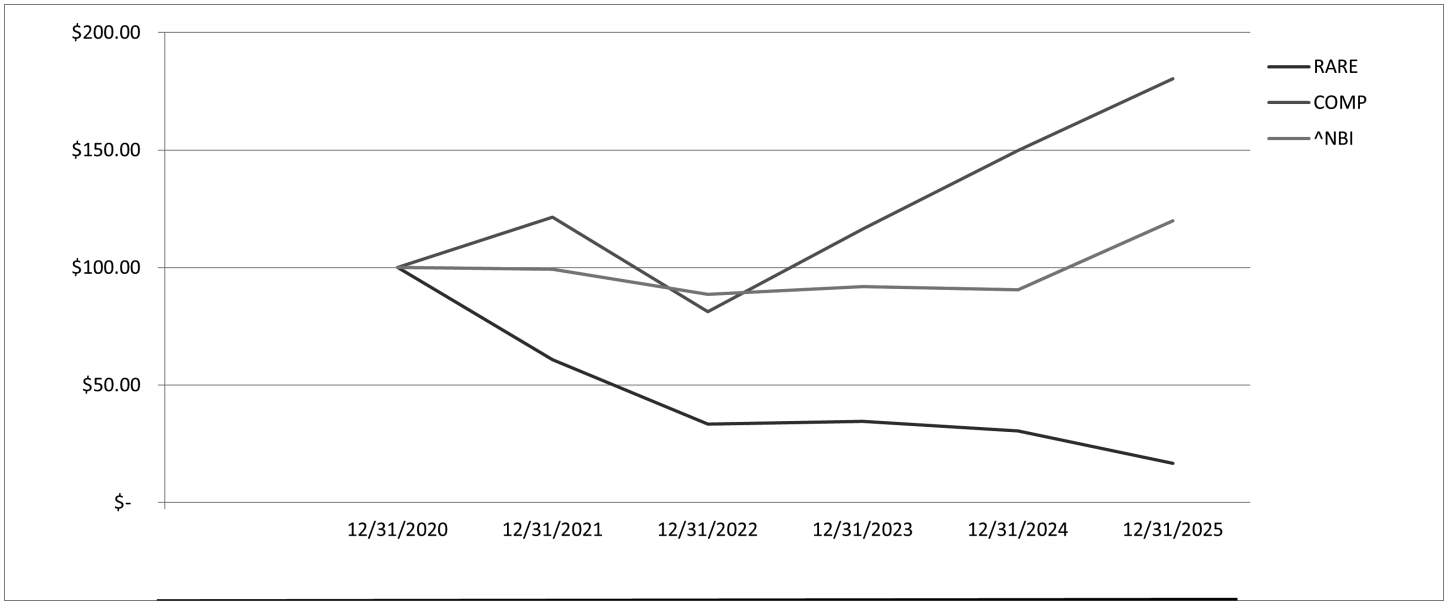
PART II

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, 2026, 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, 2020 through December 31, 2025. The figures represented below assume an investment of $100 in our common stock at the closing price of $138.43 on December 31, 2020 and in the Nasdaq Composite Index, or COMP, and the Nasdaq Biotechnology Index, or NBI, on December 31, 2020 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, 2020	December 31, 2021	December 31, 2022	December 31, 2023	December 31, 2024	December 31, 2025
Ultragenyx Pharmaceutical Inc.	RARE	$ 100.00	$ 60.75	$ 33.47	$ 34.54	$ 30.39	$ 16.61
NASDAQ Composite Index	COMP	$ 100.00	$ 121.39	$ 81.21	$ 116.47	$ 149.83	$ 180.33
NASDAQ Biotechnology Index	^NBI	$ 100.00	$ 99.37	$ 88.53	$ 91.84	$ 90.58	$ 119.92

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, 2025, including year-over-year comparisons versus the year ended December 31, 2024. Our Annual Report on Form 10-K for the year ended December 31, 2024 includes a discussion and analysis of our financial condition and results of operations for the year ended December 31, 2023 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 ultra-rare 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 $575 million and $569 million for the years ended December 31, 2025 and 2024, 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, 2025, our total revenues increased to $673 million, compared to $560 million for the same period in 2024. The increase in revenue was driven by higher demand for our approved products.

As of December 31, 2025, we had $737 million in available cash, cash equivalents and marketable 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:

Revenue Reserves

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 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 depend 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 adjustment.

Liabilities for Sales of Future Royalties

We sold our right to receive certain royalty payments from net sales of Crysvita in certain territories to RPI Finance Trust (an affiliate of Royalty Pharma) and OCM LS23 Holdings LP (an investment vehicle for Ontario Municipal Employees Retirement System, or OMERS. At inception, we recorded a liability based upon estimated future cash flows discounted at a market rate. We amortize this liability using the effective interest method over the estimated life of the applicable arrangement. To determine the amortization of the liability, we estimate the total amount of future royalty payments to be received by us and paid to RPI and OMERS. Any estimated royalty payments in excess of the initial liability are recorded as non-cash interest expense. Consequently, we estimate imputed interest on the unamortized portion of the liabilities and record as interest expense based on the estimated term of the arrangements.

We 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 our initial estimates or the timing of such payments is materially different than our original estimates, we employ the prospective method to adjust the amortization of the liabilities and the effective interest rate.

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 higher 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.

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, 2025, our total gross deferred tax assets were $1,361 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, 2025 and 2024

Revenues (dollars in millions)

	Year Ended December 31,		Dollar	Percent
	2025	2024	Change	Change
Product sales:				
Crysvita	$ 177	$ 135	$ 42	31%
Dojolvi	96	88	8	9%
Evkeeza	59	32	27	84%
Mepsevii	37	30	7	23%
Total product sales	369	285	84	29%
Crysvita royalty revenue	304	275	29	11%
Total revenues	$ 673	$ 560	$ 113	20%

Our product sales increased for the year ended December 31, 2025, compared to the same period in 2024. The increase was primarily due to increased demand for Crysvita in Latin America resulting from an increase in the number of patients on therapy, continued progress of the launch of Evkeeza in several markets in EMEA and in Japan, and the continued increase in demand for our other approved products.

Our Crysvita royalty revenue increased for the year ended December 31, 2025, compared to the same period in 2024. This increase in Crysvita revenue was primarily due to an increase in the number of patients on therapy.

Cost of Sales (dollars in millions)

	Year Ended December 31,		Dollar	Percent
	2025	2024	Change	Change
Cost of sales	$ 109	$ 77	$ 32	42%

Cost of sales increased for the year ended December 31, 2025, compared to the same period in 2024. The increase in cost of sales was primarily due to an increase in demand for Crysvita in Latin America, Evkeeza in EMEA and Japan, and the continued increase in demand for our other approved products.

Research and Development Expenses (dollars in millions)

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
	2025	2024	Change	Change
Clinical programs:				
Gene therapy programs				
DTX301	$ 27	$ 41	$ (14)	-34%
DTX401	60	75	(15)	-20%
UX701	30	33	(3)	-9%
UX111	94	41	53	129%
CMC costs	9	4	5	125%
Total gene therapy programs	220	194	26	13%
Biologic and nucleic acid programs				
GTX102	72	51	21	41%
UX143	147	89	58	65%
Total biologic and nucleic acid programs	219	140	79	56%
Translational research	39	46	(7)	-15%
Upfront license, acquisition, and milestone fees	—	30	(30)	-100%
Approved products	37	35	2	6%
Infrastructure	79	81	(2)	-2%
Stock-based compensation	84	87	(3)	-3%
Other research and development	72	85	(13)	-15%
Total research and development expenses	$ 750	$ 698	$ 52	7%

Total research and development expenses increased for the year ended December 31, 2025 compared to the same period in 2024. The change in research and development expenses was primarily due to:

- for gene therapy programs, an increase primarily due to an increase in UX111 manufacturing costs in preparation for commercial launch, partially offset by the timing of the DTX401 and DTX301 manufacturing runs for which costs were incurred during the year ended December 31, 2024, which did not recur for the year ended December 31, 2025;
- for biologic and nucleic acid programs, an increase primarily due to manufacturing costs for UX143 combined with the continued clinical conduct of the UX143 and GTX102 programs and associated clinical development and manufacturing expenses;
- for translational research, a decrease primarily due to decreases in manufacturing expense for IND-stage projects;
- for upfront license, acquisition, and milestone fees, costs for achievement of a clinical enrollment milestone on the GTX-102 program during the year ended December 31, 2024 that did not recur during the year ended December 31, 2025;
- for other research and development expenses, a decrease primarily due to decreased staffing and cost efficiencies to support internal manufacturing, and administrative and general support.

We expect a decrease in research and development expenses in the near term. This expected decline is primarily driven by the expected completion of several Phase 3 clinical programs and a strategic restructuring of our workforce and expenditures to better match our current pipeline requirements.

Selling, General and Administrative Expenses (dollars in millions)

	Year Ended December 31,		Dollar	Percent
	2025	2024	Change	Change
Selling, general and administrative	$ 349	$ 321	$ 28	9%

Selling, general and administrative expenses increased for the year ended December 31, 2025, compared to the same period in 2024. The increase was primarily due to higher employee compensation costs and increased marketing expenses as we continue to plan for our future product launches.

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

Interest Income (dollars in millions)

	Year Ended December 31,		Dollar	Percent
	2025	2024	Change	Change
Interest income	$ 25	$ 37	$ (12)	(32%)

Interest income decreased for the year ended December 31, 2025 compared to the same period in 2024, primarily due to lower marketable securities balances.

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

	Year Ended December 31,		Dollar	Percent
	2025	2024	Change	Change
Non-cash interest expense on liabilities for sales of future royalties	$ 62	$ 63	$ (1)	(2%)

The non-cash interest expense on liabilities for sales of future royalties decreased for the year ended December 31, 2025, compared to the same period in 2024, primarily due to a change in estimate related to the timing of future royalty payments from our collaboration partner, KKC. The decrease was partially offset by interest expense from the sale of future royalties to OMERS in November 2025. 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.

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, 2025, we had $737 million in available cash, cash equivalents, and marketable 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 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 November 2025, we received net proceeds of $392 million from OMERS for the sale of a percentage of our future royalties on Crysvita in the U.S. and Canada.

In June 2024, we completed an underwritten public offering for the sale of shares of common stock and pre-funded warrants. The total proceeds received from the offering were $381 million, net of underwriting discounts and commissions. As of December 31, 2025, no 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 million, from time to time, in ATM offerings through Cowen. The Company sold 2.2 million shares under the ATM for net proceeds of $80 million during the year ended December 31, 2025. No shares were sold under the ATM during the year ended December 31, 2024.

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

	Year Ended December 31,	
	2025	2024
Cash used in operating activities	$ (466)	$ (414)
Cash provided by (used in) investing activities	236	(18)
Cash provided by financing activities	478	399
Effect of exchange rate changes on cash	4	(2)
Net increase (decrease) in cash, cash equivalents, and restricted cash	$ 252	$ (35)

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, 2025 was $466 million and primarily reflected a net loss of $575 million, partially offset by non-cash items of $132 million, net, which consisted primarily of non-cash royalty revenues, non-cash interest expense related to the sale of future royalties to RPI and OMERS, stock-based compensation, amortization of discounts on marketable securities, and depreciation and amortization. The change in operating assets and liabilities also reflected a net use of cash of $23 million, primarily due to an increase in accounts receivable due to timing of sales and collections, combined with an increase in prepaid expense and other assets, primarily prepaid manufacturing, partially offset by an increase in accounts payable, accrued, and other liabilities, primarily related to an increase in accrued manufacturing in preparation for development and commercial launches.

Cash used in operating activities for the year ended December 31, 2024 was $414 million and primarily reflected a net loss of $569 million, partially offset by non-cash items of $141 million, net, which consisted primarily of non-cash royalty revenues, non-cash interest expense related to the sale of future royalties to RPI and OMERS, stock-based compensation, amortization of discounts on marketable securities, and depreciation and amortization. The change in operating assets and liabilities also reflected a net increase of cash of $14 million, primarily due to an increase in accounts payable, accrued, and other liabilities, related to an increase in accrued collaboration and higher revenue reserves from increased sales of our approved products, combined with an increase in inventory, partially offset by a decrease in prepaid expenses and other assets.

Cash Provided by (Used in) Investing Activities

Cash provided by investing activities for the year ended December 31, 2025 was $236 million and was primarily related to proceeds of $258 million from net activities in marketable securities, partially offset by $15 million in payments for intangible assets related to milestones on our commercial products.

Cash used in investing activities for the year ended December 31, 2024 was $18 million and was primarily related to $13 million in payments for intangible assets related to milestones on our commercial products, partially offset by $4 million from net activities in marketable securities.

Cash Provided by Financing Activities

Cash provided by financing activities for the year ended December 31, 2025 was $478 million and was primarily comprised of $392 million in net proceeds from the additional sale of future royalties to OMERS in November 2025, combined with $80 million in net proceeds from our ATM offering.

Cash provided by financing activities for the year ended December 31, 2024 was $399 million and was primarily comprised of $381 million in net proceeds from the sale of common stock in our June 2024 underwritten public offering and $11 million in proceeds from the issuance of common stock from exercise of equity plan awards, net.

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, sales of future royalties 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 leases and manufacturing and service contract obligations. See "Note 9. Leases" to the Consolidated Financial Statements for amounts outstanding for operating leases as of December 31, 2025.

Manufacturing and service contract obligations primarily relate to manufacturing of product for our clinical stage pipeline, the majority of which are due in the next 12 months.

Subsequent to December 31, 2025, we initiated a process to cancel certain arrangements with CMO’s related to the manufacturing of UX143. As a result, we expect that certain contract commitments will be cancelled and that the terminations will accelerate the net payments of approximately $40 million in accordance with the agreements. Our estimates are based on information available as of the approval date of the restructuring plan and are subject to change as the plan is implemented.

We generally expect to satisfy these commitments with cash on hand and cash provided by operating activities. The terms of certain of our licenses, royalties, development and collaboration agreements, as well as other research and development activities, require us to pay potential future milestone payments based on product development success. The amount and timing of such obligations are unknown or uncertain. These potential obligations are further described in "Note 8. License and Research Agreements" to the Consolidated Financial Statements.

Recent Accounting Pronouncements

See "Note 2. Summary of Significant Accounting Policies" to the Consolidated Financial Statements for a discussion of recent accounting pronouncements.

Recently Enacted Tax Legislation

The One Big Beautiful Bill Act, or OBBBA, was enacted in the U.S. in July 2025. The OBBBA legislation provides for the permanent extension of certain expiring provisions of the Tax Cuts and Jobs Act, revisions to the international tax framework and the reinstatement of favorable tax treatment for certain business provisions. The legislation has multiple effective dates, with certain provisions effective in 2025 and others implemented in future periods. We maintain a full valuation allowance against our U.S. federal and state deferred tax assets and does not anticipate achieving profitability to the extent needed to release the

valuation allowance in the near term. As such, we have determined that the OBBBA will not have a material impact on our income tax provision in the near term.

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 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, 2025, we had cash, cash equivalents, and marketable securities totaling $737 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 securities as of December 31, 2025. To date, we have not experienced a loss of principal on any of our investments and as of December 31, 2025, 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, 2025, 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, 2025. 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, 2025, 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, 2025, 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, 2025, 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, 2025, 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, 2025 and 2024, 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, 2025, and the related notes and our report dated February 18, 2026 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 18, 2026

Item 9B. *Other Information*

During the three months ended December 31, 2025, none of our directors and officers adopted a Rule 10b5-1 trading arrangement intended to satisfy the affirmative defense conditions of Rule 10b5-1(c).

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 2026 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 "2026 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 2026 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 2026 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 2026 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 2026 Proxy Statement, including under the heading "Ratification of the Selection of Independent Registered Public Accounting Firm."

PART IV

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

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

(1) Consolidated Financial Statements

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

(2) Consolidated Financial Statement Schedules

Consolidated Financial Statement schedules have been omitted in this Annual Report because they are not applicable, not required under the instructions, or the information requested is set forth in the Consolidated Financial Statements or related notes thereto.

(b) Exhibits

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
3.1	Amended and Restated Certificate of Incorporation	8-K	2/5/2014	3.1	
3.2	Second Amended and Restated Bylaws	8-K	12/21/2023	3.1	
4.1	Form of Common Stock Certificate	S-1	11/8/2013	4.2	
4.2	Form of Indenture	S-3 ASR	2/21/2024	4.2	
4.3	Form of Pre-Funded Warrant	8-K	10/23/2023	4.1	
4.4	Form of Pre-Funded Warrant	8-K	6/17/2024	4.1	
4.5	Description of Common Stock	10-K	2/14/2020	4.3	
10.1*	Collaboration and License Agreement, effective as of August 29, 2013, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	S-1/A	12/23/2013	10.1	
10.2	Amendment No. 1 to Collaboration and License Agreement, effective as of August 24, 2015, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-Q	11/10/2015	10.2	
10.3	Amendment No. 2 to Collaboration and License Agreement, effective as of November 28, 2016, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-K	2/21/2018	10.3	
10.4*	Amendment No. 3 to Collaboration and License Agreement, effective September 29, 2017, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-K	2/21/2018	10.4	
10.5*	Amendment No. 4 to Collaboration and License Agreement, effective as of January 29, 2018, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-K	2/21/2018	10.5	
10.6*	Amendment No. 5 to Collaboration and License Agreement, effective as of April 30, 2018, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-Q	8/3/2018	10.1	
10.7*	Amendment No. 6 to Collaboration and License Agreement, effective as of February 1, 2019, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-Q	5/7/2019	10.2	

10.8*	Amendment No. 7 to Collaboration and License Agreement, effective as of December 5, 2018, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-Q	5/7/2019	10.3	
10.9*	Amendment No. 8 to Collaboration and License Agreement, effective as of July 4, 2019, between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin Co., Ltd. (formerly, Kyowa Hakko Kirin Co., Ltd.)	10-Q	8/2/2019	10.1	
10.10*	Amendment No. 9 to Collaboration and License Agreement, effective December 23, 2019, between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin Co., Ltd.	10-K	2/14/2020	10.10	
10.11*	Amendment No. 10 to Collaboration and License Agreement, effective as of April 1, 2020, between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin Co., Ltd.	10-Q	5/7/2020	10.2	
10.12*	Amendment No. 11 to Collaboration and License Agreement, effective as of December 17, 2021 between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin Co., Ltd.	10-K	2/16/2022	10.13	
10.13*	Amendment No. 12 to Collaboration and License Agreement, effective as of September 29, 2022, between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin Co., Ltd.	10-Q	11/3/2022	10.1	
10.14*	Amendment No. 13 to Collaboration and License Agreement, effective as of May 16, 2023, between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin Co., Ltd.	10-Q	8/3/2023	10.1	
10.15*	Supply Agreement, effective as of November 18, 2020, between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin Inc.	10-K	2/19/2025	10.15	
10.16*	Amendment No. 1, effective as of September 13, 2024, to the Supply Agreement between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin, Inc.	10-K	2/19/2025	10.16	
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*	Royalty Purchase Agreement, dated as of November 3, 2025, by and among Rare Delaware Inc., Ultragenyx Pharmaceutical Inc. and OCM LS23 Holding LP				X
10.21#	2014 Incentive Plan (as amended)	10-K	2/17/2017	10.20	
10.22#	Form of Incentive Stock Option Agreement (2014 Plan)	S-1/A	1/17/2014	10.14	
10.23#	Form of Non Statutory Stock Option Agreement (Employees) (2014 Plan)	S-1/A	1/17/2014	10.15	
10.24#	Form of Restricted Stock Unit Agreement (Employees) (2014 Plan)	10-Q	5/10/2016	10.1	
10.25#	Form of Non-Statutory Stock Option Agreement (Annual Grant for Directors) (2014 Plan)	10-Q	8/3/2021	10.2	

10.26#	Form of Restricted Stock Unit Agreement (Annual Grant for Directors) (2014 Plan)	10-Q	8/3/2021	10.3
10.27#	Form of Non-Statutory Stock Option Agreement (Grant for New Directors) (2014 Plan)	10-Q	8/3/2021	10.4
10.28#	Form of Restricted Stock Unit Agreement (Grant for New Directors) (2014 Plan)	10-Q	8/3/2021	10.5
10.29#	Amended and Restated 2023 Incentive Plan	S-8	7/12/2024	4.4
10.30#	Form of Incentive Stock Option Agreement (2023 Plan)	10-K	2/21/2024	10.30
10.31#	Form of Non Statutory Stock Option Agreement (Employees)(2023 Plan)	10-K	2/21/2024	10.31
10.32#	Form of Restricted Stock Unit Agreement (Employees) (2023 Plan)	10-K	2/21/2024	10.32
10.33#	Form of Non-Statutory Stock Option Agreement (Annual Grant for Directors) (2023 Plan)	10-K	2/21/2024	10.33
10.34#	Form of Restricted Stock Unit Agreement (Annual Grant for Directors) (2023 Plan)	10-K	2/21/2024	10.34
10.35#	Form of Non-Statutory Stock Option Agreement (Grant for New Directors) (2023 Plan)	10-K	2/21/2024	10.35
10.36#	Form of Restricted Stock Unit Agreement (Grant for New Directors) (2023 Plan)	10-K	2/21/2024	10.36
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)	10-K	2/19/2025	10.38
10.39#	Form of Performance Stock Unit Agreement (2025)	10-Q	5/6/2025	10.1
10.40#	Amended and Restated 2014 Employee Stock Purchase Plan	S-8	6/8/2023	4.5
10.41#	Corporate Bonus Plan	S-1/A	1/17/2014	10.27
10.42#	Employment Inducement Plan	10-K	2/12/2021	10.43
10.43#	First Amendment to Employment Inducement Plan	S-8	6/8/2023	4.7
10.44#	Second Amendment to Employment Inducement Plan	S-8	7/12/2024	4.7
10.45#	Third Amendment to Employment Inducement Plan	S-8	7/18/2025	4.8
10.46#	Form of Non Statutory Stock Option Agreement (Inducement Plan)	10-K	2/12/2021	10.44
10.47#	Form of Non Statutory Stock Option Agreement (Inducement Plan) (ex-US)	10-K	2/12/2021	10.45
10.48#	Form of Restricted Stock Unit Agreement (Inducement Plan)	10-K	2/12/2021	10.46
10.49#	Form of Restricted Stock Unit Agreement (Inducement Plan)(ex-US)	10-K	2/12/2021	10.47
10.50#	Ultragenyx Pharmaceutical Inc. Deferred Compensation Plan	10-Q	8/3/2021	10.1
10.51#	Amendment No. 1 to the Ultragenyx Pharmaceutical Inc. Deferred Compensation Plan	10-Q	11/3/2021	10.1
10.52#	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

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

10.71	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
10.72	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
10.73	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
10.74	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
10.75	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
10.76	Addendum #7 to Standard Lease, effective as of November 22, 2024, between Ultragenyx Pharmaceutical Inc. and Condiotti Enterprises, Inc.	10-K	2/19/2025	10.77
10.77	Lease Agreement, dated as of December 8, 2015, between Marina Boulevard Property, LLC and Ultragenyx Pharmaceutical Inc.	10-K	2/26/2016	10.43
10.78	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
10.79	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
10.80	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
10.81	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
10.82	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
10.83	Fifth Amendment, dated November 25, 2024, to the Lease Agreement between Ultragenyx Pharmaceutical Inc. and ARE-MA Region No. 20, LLC	10-K	2/19/2025	10.84
10.84	Lease Agreement, dated December 15, 2019, between Ultragenyx Pharmaceutical Inc. and ARE-San Francisco No. 17, LLC.	10-K	2/12/2021	10.81
10.85	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
10.86	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

10.87	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	
10.88	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)	10-K	2/19/2025	10.89	
10.89	Office Lease, dated April 19, 2019, between Ultragenyx Pharmaceutical Inc. and Woburn MCB II, LLC	10-K	2/14/2020	10.70	
10.90	First Amendment, dated December 9, 2025, to the Lease Agreement between Ultragenyx Pharmaceutical Inc. and Woburn MCB II, LLC				X
10.91	Lease, dated August 18, 2022, between Ultragenyx Pharmaceutical Inc. and Brickbottom I QOZB L.P.	10-K	2/17/2023	10.95	
10.92	First Amendment, dated March 12, 2024, between Ultragenyx Pharmaceutical Inc. and Brickbottom I QOZB L.P.	10-K	2/19/2025	10.93	
10.93	Commercial Lease, dated July 2, 2018, between Ultragenyx Pharmaceutical Inc. and 32 Leveroni LLC	10-K	2/14/2020	10.71	
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 18, 2026

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 18, 2026
/s/ Howard Horn Howard Horn	Executive Vice President, Chief Financial Officer, Corporate Strategy (Principal Financial Officer)	February 18, 2026
/s/ Theodore A. Huizenga Theodore A. Huizenga	Senior Vice President and Chief Accounting Officer (Principal Accounting Officer)	February 18, 2026
/s/ Daniel G. Welch Daniel G. Welch	Chairman of the Board	February 18, 2026
/s/ Deborah Dunsire Deborah Dunsire, M.D.	Director	February 18, 2026
/s/ Matthew K. Fust Matthew K. Fust	Director	February 18, 2026
/s/ Michael Narachi Michael Narachi	Director	February 18, 2026
/s/ Amrit Ray Amrit Ray, M.D.	Director	February 18, 2026
/s/ Corsee D. Sanders Corsee D. Sanders, Ph.D.	Director	February 18, 2026
/s/ Shehnaaz Suliman Shehnaaz Suliman, M.D.	Director	February 18, 2026

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, 2025 and 2024, 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, 2025, 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, 2025 and 2024, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2025, 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, 2025, 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 18, 2026 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 10, the Company has entered into three 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, $500 million and $400 million.

The proceeds from each transaction were recorded as liabilities and are being amortized using the effective interest method over the estimated lives of the respective arrangements. 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 counterparties, subject to capped amount. 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 challenging because it required significant judgment to evaluate management's forecasts of expected royalty payments, which are dependent on forward-looking assumptions.

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 future royalties and the imputed effective interest rates, we performed audit procedures that included, among others, evaluating the reasonableness of management's assumptions related to forecasted royalty growth rates. We compared management's forecasted royalty payments to historical trends and to analyst expectations for underlying Crysvita sales. We also performed a sensitivity analysis over the estimated future royalties to assess the impact of changes in key assumptions on the interest expense recorded for the year ended December 31, 2025.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2012.

San Mateo, California
February 18, 2026

ULTRAGENYX PHARMACEUTICAL INC.

CONSOLIDATED BALANCE SHEETS
(in millions, except per share amounts)

	December 31,	
	2025	**2024**
ASSETS		
Current assets:		
Cash and cash equivalents	$ 421	$ 174
Marketable securities	259	436
Accounts receivable, net	158	122
Inventory	52	45
Prepaid expenses and other assets	61	40
Total current assets	951	817
Property, plant, and equipment, net	244	266
Marketable securities	57	135
Intangible assets, net	176	178
Goodwill	44	44
Other assets	60	63
Total assets	$ 1,532	$ 1,503
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 31	$ 39
Accrued liabilities	265	241
Lease liabilities	12	10
Liabilities for sales of future royalties	69	50
Other liabilities	7	4
Total current liabilities	384	344
Lease liabilities	24	30
Deferred tax liabilities	30	30
Liabilities for sales of future royalties	1,147	820
Other liabilities	20	17
Total liabilities	1,605	1,241
Commitments and contingencies (Note 15)		
Noncontrolling interest	7	7
Stockholders' equity (deficit):		
Preferred stock, par value of $0.001 per share—25.0 shares authorized; nil outstanding in 2025 and in 2024	—	—
Common stock, par value of $0.001 per share—250.0 shares authorized; outstanding—96.6 in 2025 and 92.5 in 2024	—	—
Treasury stock, at cost, 0.2 shares in 2025 and 0.1 shares in 2024	(8)	(4)
Deferred compensation obligation	8	4
Additional paid-in capital	4,451	4,213
Accumulated other comprehensive income (loss)	1	(1)
Accumulated deficit	(4,532)	(3,957)
Total stockholders' equity (deficit)	(80)	255
Total liabilities, noncontrolling interest and stockholders' equity (deficit)	$ 1,532	$ 1,503

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

CONSOLIDATED STATEMENTS OF OPERATIONS
(in millions, except per share amounts)

	Year Ended December 31,		
	2025	**2024**	**2023**
Revenues:			
Product sales	$ 369	$ 285	$ 180
Royalty revenue	304	275	183
Collaboration and license	—	—	71
Total revenues	673	560	434
Operating expenses:			
Cost of sales	109	77	45
Research and development	750	698	648
Selling, general and administrative	349	321	310
Total operating expenses	1,208	1,096	1,003
Loss from operations	(535)	(536)	(569)
Interest income	25	37	27
Non-cash interest expense on liabilities for sales of future royalties	(62)	(63)	(66)
Other income (expense)	1	(5)	(1)
Loss before income taxes	(571)	(567)	(609)
(Provision for) benefit from income taxes	(4)	(2)	2
Net loss	$ (575)	$ (569)	$ (607)
Net loss per share, basic and diluted	$ (5.83)	$ (6.29)	$ (8.25)
Shares used in computing net loss per share, basic and diluted	98.6	90.5	73.5

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(in millions)

	Year Ended December 31,		
	2025	**2024**	**2023**
Net loss	$ (575)	$ (569)	$ (607)
Other comprehensive income (loss):			
Foreign currency translation adjustments	3	(2)	—
Change in unrealized gain (loss) on available-for-sale securities	(1)	—	8
Other comprehensive income (loss):	2	(2)	8
Total comprehensive loss	$ (573)	$ (571)	$ (599)

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)

(In millions)	Common Stock Shares	Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Treasury Stock	Deferred Compensation Obligation	Total Stockholders' Equity (Deficit)
Balance as of December 31, 2022	70.2	$ 3,140	$ (7)	$ (2,781)	$ —	$ —	$ 352
Issuance of common stock and pre-funded warrants in connection with underwritten public offering, net of issuance costs	9.8	326	—	—	—	—	326
Issuance of common stock in connection with at-the-market offering, net of issuance costs	1.2	53	—	—	—	—	53
Stock-based compensation	—	135	—	—	—	—	135
Issuance of common stock under equity plan awards, net of tax	1.1	8	—	—	—	—	8
Other comprehensive income	—	—	8	—	—	—	8
Net loss	—	—	—	(607)	—	—	(607)
Balance as of December 31, 2023	82.3	$ 3,662	$ 1	$ (3,388)	$ —	$ —	$ 275
Issuance of common stock and pre-funded warrants in connection with underwritten public offering, net of issuance costs	8.8	381	—	—	—	—	381
Stock-based compensation	—	159	—	—	—	—	159
Issuance of common stock under equity plan awards, net of tax	1.4	11	—	—	—	—	11
Deferred compensation	—	—	—	—	(4)	4	—
Other comprehensive loss	—	—	(2)	—	—	—	(2)
Net loss	—	—	—	(569)	—	—	(569)
Balance as of December 31, 2024	92.5	$ 4,213	$ (1)	$ (3,957)	$ (4)	$ 4	$ 255
Issuance of common stock in connection with at-the-market offering, net	2.2	80	—	—	—	—	80
Stock-based compensation	—	152	—	—	—	—	152
Issuance of common stock under equity plan awards, net of tax	1.9	6	—	—	—	—	6
Deferred compensation	—	—	—	—	(4)	4	—
Other comprehensive income	—	—	2		—	—	2
Net loss	—	—	—	(575)	—	—	(575)
Balance as of December 31, 2025	96.6	$ 4,451	$ 1	$ (4,532)	$ (8)	$ 8	$ (80)

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(in millions)

	Year Ended December 31,		
	2025	**2024**	**2023**
Operating activities:			
Net loss	$ (575)	$ (569)	$ (607)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	153	158	135
Amortization of discount on marketable securities, net	(4)	(13)	(13)
Depreciation and amortization	35	36	26
Non-cash royalty revenue	(112)	(101)	(69)
Non-cash interest expense on liabilities for sales of future royalties	62	63	66
Other	(2)	(2)	3
Changes in operating assets and liabilities:			
Accounts receivable	(31)	(34)	(23)
Inventory	(6)	(11)	(7)
Prepaid expenses and other assets	(10)	12	15
Accounts payable, accrued, and other liabilities	24	47	(1)
Net cash used in operating activities	(466)	(414)	(475)
Investing activities:			
Purchase of property, plant, and equipment	(6)	(7)	(44)
Purchase of marketable securities	(186)	(409)	(526)
Proceeds from sale of marketable securities	—	3	51
Proceeds from maturities of marketable securities	444	410	696
Payments for intangible asset	(15)	(13)	(3)
Other	(1)	(2)	(6)
Net cash provided by (used in) investing activities	236	(18)	168
Financing activities:			
Proceeds from the sale of future royalties, net	392	—	—
Proceeds from the issuance of common stock and pre-funded warrants in connection with underwritten public offerings, net	—	381	326
Proceeds from the issuance of common stock in connection with at-the-market offering, net	80	—	53
Proceeds from the issuance of common stock under equity plans, net	6	11	8
Proceeds from issuance of equity from noncontrolling interest	—	7	—
Other	—	—	1
Net cash provided by financing activities	478	399	388
Effect of exchange rate changes on cash	4	(2)	—
Net increase (decrease) in cash, cash equivalents, and restricted cash	252	(35)	81
Cash, cash equivalents, and restricted cash at beginning of year	184	219	138
Cash, cash equivalents, and restricted cash at end of year	$ 436	$ 184	$ 219

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(in millions)

	Year Ended December 31,		
	2025	**2024**	**2023**
Supplemental disclosures of non-cash information:			
Acquired lease liabilities arising from obtaining right-of-use assets and property, plant, and equipment	$ 6	$ 10	$ 22
Non-cash interest expense on liabilities for sales of future royalties capitalized during the year into ending property, plant and equipment	$ —	$ —	$ 9
Costs of intangible assets included in accounts payable, accrued and other liabilities	$ 5	$ 15	$ 10

See accompanying notes.

1. Organization and Basis of Presentation

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

The Company is focused on the identification, acquisition, development, and commercialization of novel products for the treatment of serious rare and ultra-rare genetic diseases. The Company operates as one reportable segment and has four commercially approved products.

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

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

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

Evkeeza® (evinacumab) is approved in the U.S. and the European Economic Area, or EEA, 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;
- 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;
- 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;
- UX701 is an adeno-associated virus 9, or AAV9, gene therapy designed to deliver stable expression of a truncated version of the ATP7B copper transporter following a single intravenous infusion to improve copper distribution and excretion from the body and reverse pathological findings of Wilson liver disease; and
- UX143 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.

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, 2025, the Company has relied primarily on the sale of equity securities, revenues from commercial products, the sale of certain 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. Certain reclassifications have been made to prior periods in the consolidated financial statements and accompanying notes to conform with the current presentation.

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, is the Company's Chief Executive Officer. The CODM manages the Company's operations on an integrated basis for the purpose 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 consolidated 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 millions):

	December 31,		
	2025	2024	2023
Cash and cash equivalents	$ 421	$ 174	$ 214
Restricted cash included in other current assets	13	7	2
Restricted cash included in other non-current assets	2	3	3
Total cash, cash equivalents, and restricted cash shown in the statements of cash flows	$ 436	$ 184	$ 219

Marketable Securities

All marketable 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 securities and investments with a maturity of greater than one year from the balance sheet date are reported as non-current marketable 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. There were no material credit losses recorded for receivables and available-for-sale debt securities which were attributable to credit risk for the years ended December 31, 2025 and 2024.

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, 2025 and 2024.

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 in conjunction with license agreements and collaboration agreements. 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 10. Liabilities for Sales of Future Royalties." At inception, the Company recorded a liability based upon estimated future cash flows discounted at a market rate. The liability is amortized using the effective interest method over the estimated life of the applicable arrangement. To determine the amortization of the liability, the Company estimates the total amount of future royalty payments to be received by the Company and paid to RPI and OMERS. Any estimated royalty payments in excess of the initial liability are recorded as non-cash interest expense. Consequently, the Company estimates imputed interest on the unamortized portion of the liabilities and records interest expense based on the estimated term of the arrangements.

The Company periodically assesses the expected royalty payments using a combination of historical results, internal projections and forecasts from external sources. To the extent such payments are greater or less than the Company's initial estimates or the timing of such payments is materially different than its original estimates, the Company 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 depend 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 the license of intellectual property.

As described in "Note 10. 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 non-cash royalty revenue on a prospective basis as 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 (deficit).

Leases

Lease agreements are evaluated to determine whether an arrangement is or contains a lease in accordance with ASC 842, *Leases*. The Company determines if an arrangement includes a lease at inception. Right-of-use lease assets and lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term at the commencement date. The right-of-use lease asset includes any lease payments made and excludes lease incentives. Incremental borrowing rate is used in determining the present value of future payments. The Company applies a portfolio approach to the property leases to apply an incremental borrowing rate to leases with similar lease terms. The lease terms may include options to extend or terminate the lease. The Company recognizes the options to extend the lease as part of the right-of-use lease assets and lease liabilities only if it is reasonably certain that the option would be exercised. Lease expense for minimum lease payments is recognized on a straight-line basis over the non-cancelable lease term. The Company has elected to not separate lease and non-lease components. See "Note 9. Leases" for further disclosure.

Comprehensive Loss

Comprehensive loss is the change in stockholders' equity (deficit) from transactions and other events and circumstances other than those resulting from investments by stockholders and distributions to stockholders. The Company's other comprehensive loss is comprised of unrealized gains and losses on investments in available-for-sale securities 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 December 2023, the FASB issued ASU 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures* requiring public entities to disclose disaggregated information about their effective tax rate reconciliation and additional information about income taxes paid. Disclosure requirements will be applied on a prospective basis. ASU 2023-09 is effective for fiscal years beginning after December 15, 2024. The Company adopted ASU 2023-09 during the year ended December 31, 2025.

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 and liabilities remeasured on a recurring basis based on the three-tier fair value hierarchy (in millions):

	December 31, 2025			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 320	$ —	$ —	$ 320
Time deposits	—	10	—	10
Corporate bonds	—	263	—	263
Commercial paper	—	37	—	37
U.S. Government Treasury and agency securities	12	23	—	35
Investment in Solid common stock	3	—	—	3
Deferred compensation assets	—	19	—	19
Total financial assets	$ 335	$ 352	$ —	$ 687
Financial Liabilities:				
Deferred compensation liabilities	$ —	$ 19	$ —	$ 19

	December 31, 2024			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 114	$ —	$ —	$ 114
Time deposits	—	10	—	10
Corporate bonds	—	392	—	392
Commercial paper	—	21	—	21
U.S. Government Treasury and agency securities	—	159	—	159
Investment in Solid common stock	2	—	—	2
Deferred compensation assets	—	15	—	15
Total financial assets	$ 116	$ 597	$ —	$ 713
Financial Liabilities:				
Deferred compensation liabilities	$ —	$ 16	$ —	$ 16

Deferred compensation liabilities consist of short-term liabilities of $1 million and $1 million as of December 31, 2025 and 2024, respectively, included in accrued liabilities on the Consolidated Balance Sheets, and long-term liabilities of $18 million and $15 million as of December 31, 2025 and 2024, respectively, included in other non-current liabilities on the Consolidated Balance Sheets. There have been no material net gains or losses on deferred compensation assets or liabilities for the periods presented.

4. Balance Sheet Components

Cash Equivalents and Marketable Securities

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

	December 31, 2025			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Money market funds	$ 320	$ —	$ —	$ 320
Time deposits	10	—	—	10
Corporate bonds	263	—	—	263
Commercial paper	37	—	—	37
U.S. Government Treasury and agency securities	35	—	—	35
Total	$ 665	$ —	$ —	$ 665

	December 31, 2024			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Money market funds	$ 114	$ —	$ —	$ 114
Time deposits	10	—	—	10
Corporate bonds	391	1		392
Commercial paper	21	—	—	21
U.S. Government Treasury and agency securities	159	—	—	159
Total	$ 695	$ 1	$ —	$ 696

At December 31, 2025, the remaining contractual maturities of available-for-sale securities were less than two years. The cost of securities sold is based on the specific-identification method. 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, 2025 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 millions):

	December 31,	
	2025	2024
Work-in-process	$ 27	$ 22
Finished goods	25	23
Total inventory	$ 52	$ 45

Property, Plant, and Equipment, net

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

		December 31,	
	Useful life (years)	2025	2024
Building	20-30	$ 182	$ 182
Leasehold improvements	Shorter of lease term or estimated useful life	55	58
Research and development equipment	5	65	60
Furniture and office equipment	5	7	6
Computer equipment and software	3-5	16	16
Manufacturing equipment	5-15	37	37
Land	Not applicable	17	17
Other	Varies by asset	1	2
Property, plant, and equipment, gross		380	378
Less: accumulated depreciation		(136)	(112)
Property, plant, and equipment, net		$ 244	$ 266

Depreciation expense for the years ended December 31, 2025, 2024, and 2023 was $27 million, $30 million and $22 million, respectively. Amortization of leasehold improvements and software is included in depreciation expense.

Accrued Liabilities

Accrued liabilities consist of the following (in millions):

	December 31,	
	2025	2024
Research and clinical study expenses	$ 23	$ 24
Payroll and related expenses	89	94
Revenue related reserves	57	33
Manufacturing and related expenses	67	25
Commercial and development milestones	5	45
Other	24	20
Total accrued liabilities	$ 265	$ 241

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 million as of December 31, 2025 and 2024. 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 $5 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 entered into 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 $63 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 (in millions, except for years):

	December 31, 2025			
	Gross Carrying Amount	Weighted-Average Life (Years)	Accumulated Amortization	Net Carrying Amount
Indefinite-lived intangibles	$ 129	—	$ —	$ 129
Finite-lived intangibles	68	9	(21)	47
Total intangible assets	$ 197	—	$ (21)	$ 176

	December 31, 2024			
	Gross Carrying Amount	Weighted-Average Life (Years)	Accumulated Amortization	Net Carrying Amount
Indefinite-lived intangibles	$ 129	—	$ —	$ 129
Finite-lived intangibles	62	9	(13)	49
Total intangible assets	$ 191	—	$ (13)	$ 178

The Company recorded costs of sales of $8 million, $6 million and $4 million for the years ended December 31, 2025, 2024, and 2023, respectively, related to the amortization of intangible assets.

The expected amortization of intangible assets, as of December 31, 2025, for each of the next five years and thereafter is as follows (in millions):

2026	$ 8
2027	7
2028	7
2029	7
2030	7
Thereafter	11
Total	$ 47

6. Revenue

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

	Year Ended December 31,		
	2025	2024	2023
Product sales:			
Crysvita	$ 177	$ 135	$ 75
Dojolvi	96	88	71
Evkeeza	59	32	4
Mepsevii	37	30	30
Total product sales	369	285	180
Crysvita royalty revenue	304	275	183
Collaboration and license revenue:			
Crysvita collaboration revenue in Profit-Share Territory	—	—	70
Other	—	—	1
Total collaboration and license revenue	—	—	71
Total revenues	$ 673	$ 560	$ 434

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

	Year Ended December 31,		
	2025	2024	2023
North America	$ 377	$ 340	$ 307
Latin America	170	131	77
Europe, Middle East, and Africa	108	80	48
Asia-Pacific	18	9	2
Total revenues	$ 673	$ 560	$ 434

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

	Year Ended December 31,		
	2025	2024	2023
Balance of product sales reserve at beginning of year	$ 33	$ 17	$ 11
Provisions	50	38	19
Payments	(30)	(21)	(13)
Adjustments	4	(1)	—
Balance of product sales reserve at end of year	$ 57	$ 33	$ 17

The Company's largest accounts receivable balance was from a collaboration partner, KKC, and was 62% and 70% of the total accounts receivable balance as of December 31, 2025 and 2024, 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 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, 2025 and 2024, total assets included on the Consolidated Balance Sheets for Amlogenyx were $5 million and $14 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, 2025, were as follows (in millions):

	Noncontrolling Interest
As of December 31, 2023	$ —
Issuance of equity from noncontrolling interest	7
As of December 31, 2024	$ 7
Changes and adjustments	—
As of December 31, 2025	$ 7

8. License and Research Agreements

Kyowa Kirin Co., Ltd.

In August 2013, the Company entered into a collaboration and license agreement with Kyowa Kirin Co., Ltd., or KKC. 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 Türkiye

The Company is responsible for commercializing Crysvita in Latin America and Türkiye. 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 Türkiye, 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 Türkiye. KKC charges the Company a transfer price of 30% of net sales for supply of product to Latin America. 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. 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%.

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, beginning in April 2023, that are due to the Company based on net sales of Crysvita in the U.S. and Canada, subject to a cap. In November 2025, the Company sold to OMERS its right to an additional 25% of the future royalty payments, beginning in January 2028, that are due to the Company based on net sales of Crysvita in the U.S. and Canada, subject to a cap. These agreements are further described in "Note 10. Liabilities for Sales of Future Royalties."

Royalty Revenue for Sales in the European Territory

KKC has commercial responsibility for Crysvita in the European Territory. Under the collaboration agreement, the Company is entitled to receive royalties of up to 10% of net sales in the European Territory, which are recorded as royalty revenue as the underlying sales occur. In December 2019, the Company sold its right to receive these royalty payments to Royalty Pharma, effective January 1, 2020, as further described in "Note 10. Liabilities for Sales of Future Royalties."

Total Crysvita revenue was as follows (in millions):

	Year Ended December 31,		
	2025	2024	2023
Product sales	$ 177	$ 135	$ 75
Revenue in Profit-Share Territory:			
Royalty revenue	192	174	113
Non-cash royalty revenue	83	75	49
Collaboration revenue	—	—	70
Total revenue in Profit-Share Territory	275	249	232
Non-cash royalty revenue in European Territory	29	26	21
Total Crysvita revenue	$ 481	$ 410	$ 328

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 Consolidated Statements of Operations in connection with the collaboration agreement with KKC as follows (in millions):

	Year Ended December 31,		
	2025	2024	2023
Research and development	$ (5)	$ (4)	$ (7)
Selling, general and administrative	$ —	$ (4)	$ (17)
Cost of sales	$ 61	$ 46	$ 18

Collaboration Receivable and Payable

The Company had accounts receivable from KKC in the amount of $98 million and $85 million from royalties, other receivables of $1 million and $2 million recorded in other current assets, and accrued liabilities of $12 million and $7 million from amounts owed for transfer price and royalties as well as commercial and development activity reimbursements, as of December 31, 2025 and 2024, respectively.

Regeneron

In January 2022, the Company entered into 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 million upfront payment. As of December 31, 2025, the Company has recognized an aggregate of $33 million for regulatory and sales milestones under the agreement. 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. The Company is required to pay up to an aggregate of $31 million in the future contingent upon the achievement of certain regulatory and sales milestones. The Company may share in certain costs for global trials led by Regeneron. Additionally, the Company pays Regeneron a product purchase price 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 product purchase price from the low 20% range up to 40% on net sales, which is recognized as cost of sales in the Company's Consolidated Statement of Operations.

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

	Year Ended December 31,		
	2025	2024	2023
Research and development	$ 1	$ (3)	$ 8
Cost of sales	$ 16	$ 8	$ 1

The Company had collaboration payables for this arrangement included in accrued liabilities on the Consolidated Balance Sheets of $9 million and $18 million as of December 31, 2025 and 2024, 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 million contingent upon achievement of development and regulatory milestones as well as royalties in the low single-digits of net sales.

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., Türkiye, 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 million to Mereo. As of December 31, 2025, the Company has made payments totaling $9 million for regulatory milestones achieved. The Company is obligated to pay Mereo up to $245 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 priority review voucher, or 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 for reimbursing 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 years ended December 31, 2025 and 2024, the Company recorded offsets to research and development expense of $5 million and $1 million, respectively. For the year ended December 31, 2023, the Company recorded development costs of $9 million for the achievement of a clinical milestone recorded in research and development expense.

As of December 31, 2025 and 2024, the Company had receivables from Mereo in the amount of $1 million and $1 million, respectively, recorded in other current assets for development activity reimbursements.

GeneTx Biotherapeutics LLC

In August 2019, the Company entered into a Program Agreement and a Unitholder Option Agreement with GeneTx Biotherapeutics LLC, or GeneTx, as subsequently amended, or the Option Agreement, to collaborate on the development of GeneTx's GTX-102, an ASO for the treatment of Angelman syndrome. In July 2022, the Company exercised its option to acquire GeneTx, pursuant to the terms of the Option Agreement. During the year ended December 31, 2024, the Company achieved a $30 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 million in additional regulatory approval milestones for the achievement of U.S. and EU product approvals, and up to $75 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 chooses 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. The Company recognized an aggregate of $1 million for clinical milestones under the TAMU agreement, and has future obligations up to $23 million for various milestones and a nominal annual license fee that may increase up to a maximum of $2 million. The Company will also pay mid-single-digit percentage royalties based on licensed product annual net sales. As of December 31, 2025 and 2024, the Company had nil and $1 million, respectively, in collaboration payables under this arrangement.

Prior to the achievement of certain development and regulatory milestones, amounts paid towards the milestones are classified as in-process research and development expense, as the acquired in-process research and development intangible asset has not yet reached technological feasibility and has no alternative future use.

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 million for each indication, if certain development milestones are achieved. The Company is also obligated to make milestone payments of up to $25 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. This license agreement was terminated for certain indications in November 2025.

The Company also had an option and license agreement with REGENX under which the Company had 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. This option and license agreement was terminated in November 2025.

9. 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 2031. 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 millions):

	Year Ended December 31,		
	2025	2024	2023
Operating lease expense	$ 12	$ 12	$ 13
Variable lease expense	5	6	5
Total	$ 17	$ 18	$ 18

Cash paid for amounts included in the measurement of operating lease liabilities for the years ended December 31, 2025, 2024, and 2023 was $14 million, $16 million, and $13 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 $23 million and $26 million as of December 31, 2025 and 2024, 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, 2025 (in millions):

Year Ending December 31,	Operating
2026	$ 15
2027	10
2028	8
2029	7
2030	2
Thereafter	1
Total future lease payments	43
Less: Amount representing interest	(7)
Present value of future lease payments	36
Less: Lease liabilities, current	(12)
Lease liabilities, non-current	$ 24

For the years ended December 31, 2025 and 2024, the weighted-average remaining operating lease terms and the weighted-average discount rates used to determine the lease liability were as follows:

	Year Ended December 31,	
	2025	2024
Weighted-average remaining lease term (in years)	4	4
Weighted-average discount rate	10.0%	10.1%

10. Liabilities for Sales of Future Royalties

In December 2019, the Company entered into a Royalty Purchase Agreement with RPI. Pursuant to the agreement, RPI paid $320 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 million prior to December 31, 2030, or when aggregate royalty payments received by RPI are equal to $800 million.

In July 2022, the Company entered into a Royalty Purchase Agreement with OMERS, or the 2022 OMERS Agreement. Pursuant to the agreement, OMERS paid $500 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 million or on the date the final royalty payment is made to the Company under the KKC Collaboration Agreement.

In November 2025, the Company entered into a second Royalty Purchase Agreement with OMERS, or the 2025 OMERS Agreement. Pursuant to the agreement, OMERS paid $400 million to the Company in exchange for the right to receive an additional 25% of future royalty payments, starting on January 1, 2028, on net sales of Crysvita in the U.S. and Canada. OMERS will also continue to receive 30% of Crysvita net sales in the U.S. and Canada following the achievement of $725 million in aggregate payments under the 2022 OMERS Agreement. The 2025 OMERS Agreement will expire upon the earlier of the date on which aggregate payments received by OMERS under this transaction equal $620 million or on the date the final royalty payment is made to the Company under the KKC Collaboration Agreement. Under the agreement, OMERS granted the Company an option to repurchase the entire purchased interest, that expires in November 2027, for 1.35 times the purchase price, or $540 million.

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 liabilities of $320 million, $500 million, and $400 million, net of transaction costs of $6 million, $9 million, and $8 million, for the RPI Agreement, the 2022 OMERS Agreement, and the 2025 OMERS Agreement, 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 Agreement, the 2022 OMERS Agreement, and the 2025 OMERS Agreement from inception to December 31, 2025 have been $128 million, $206 million, and nil, respectively. The Company's effective annual interest rates were 5.5%, 7.3%, and 9.2% for the RPI Agreement, the 2022 OMERS Agreement, and the 2025 OMERS Agreement, respectively, as of December 31, 2025.

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 millions):

	Liabilities for Sales of Future Royalties			
	RPI	OMERS 2022	OMERS 2025	Total
December 31, 2023	$ 377	$ 515	$ —	$ 892
Royalty revenue	(26)	(59)	—	(85)
Non-cash interest expense	24	39	—	63
December 31, 2024	375	495	—	870
Net proceeds from sale of future royalties	—	—	392	392
Royalty revenue	(29)	(79)	—	(108)
Non-cash interest expense	20	36	6	62
December 31, 2025	$ 366	$ 452	$ 398	$ 1,216

11. 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 of up to $350 million, from time to time, in at-the-market, or ATM, offerings through Cowen. The Company sold 2.2 million shares under the ATM for net proceeds of $80 million during the year ended December 31, 2025.

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 of up to $350 million, from time to time, in ATM offerings through Jefferies. During the year ended December 31, 2023, there were 1.2 million shares sold under the ATM resulting in net proceeds of $53 million.

Underwritten Public Offering

In June 2024, the Company completed an underwritten public offering in which 8.8 million shares of common stock were sold, including the exercise in full by the underwriters of their option to purchase an additional 1.3 million 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 1.5 million 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 million, net of underwriting discounts and commissions.

In October 2023, the Company completed an underwritten public offering in which 9.8 million shares of common stock were sold, including the exercise in full by the underwriters of their option to purchase an additional 1.5 million 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 1.7 million 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 $327 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, 2025, no pre-funded warrants had been exercised.

The table below summarizes pre-funded warrants activity:

	Pre-funded warrants (millions)
As of December 31, 2023	1.7
Issuance of pre-funded warrants	1.5
As of December 31, 2024	3.2
Changes and adjustments	—
As of December 31, 2025	3.2

12. 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, 2025, the Company issued 0.2 million shares of common stock under the ESPP.

The table below summarizes the Company's equity plans as of December 31, 2025:

Plan	Year of Adoption	Expiration Date, as Amended	Maximum Number of Shares Authorized (millions)	Shares Available for Future Issuance (millions)
Employment Inducement Plan	2021	February 3, 2031	1.7	0.3
2023 Incentive Plan[(1)]	2023	June 7, 2033	15.5	7.9
2014 Employee Stock Purchase Plan	2014	June 7, 2033	7.3	6.2

(1) Maximum number of shares authorized and shares available for future issuance under the 2023 Incentive Plan includes 4.0 million 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 (millions)	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (In millions)
Outstanding — December 31, 2024	9.4	$ 65.54	6	$ 2
Options granted	1.2	41.75		
Options exercised	—	38.57		
Options cancelled	(1.7)	73.53		
Outstanding — December 31, 2025	8.9	60.87	6	—
Vested and exercisable — December 31, 2025	6.5	66.31	5	—
Vested and expected to vest — December 31, 2025	8.7	61.24	6	—

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

	Year Ended December 31,		
	2025	2024	2023
Intrinsic value of options exercised	$ —	$ 1	$ 5
Cash received from the exercise of options	$ —	$ 6	$ 3
Weighted-average estimated fair value of options granted	$ 22.92	$ 29.88	$ 25.53
Estimated fair value of options vested	$ 46	$ 54	$ 60

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 (millions)	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding — December 31, 2024	1.2	$ 67.37	2	$ —
PSOs cancelled	(0.4)	67.37		
Outstanding — December 31, 2025	0.8	67.37	1	—
Vested and exercisable — December 31, 2025	0.8	67.37	1	—
Vested and expected to vest — December 31, 2025	0.8	67.37	1	—

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, 2025, certain operational milestones had been achieved. 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, 2025, 2024, and 2023 was $14 million, $10 million, and $3 million, respectively.

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 (millions)	Weighted-Average Grant Date Fair Value
Unvested — December 31, 2024	5.2	$ 53.22
RSUs granted	2.9	41.04
RSUs vested	(1.5)	56.39
RSUs cancelled	(0.7)	49.78
Unvested — December 31, 2025	5.9	46.23

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, 2025, 2024, and 2023 was $85 million, $63 million, and $55 million, respectively. The aggregate intrinsic value of the shares of the RSUs vested during the years ended December 31, 2025, 2024, and 2023 was $62 million, $54 million, and $33 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 (millions)	Weighted-Average Grant Date Fair Value
Unvested — December 31, 2024	0.6	$ 59.39
PSUs granted	0.4	50.77
PSUs vested	(0.2)	53.44
PSUs cancelled	(0.1)	49.95
Unvested — December 31, 2025	0.7	57.48

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, 2025, 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, 2025, 2024, and 2023 was $12 million, $3 million, and $4 million, respectively, with an aggregate intrinsic value of the shares of $9 million, $2 million and $1 million, respectively.

Stock-Based Compensation Expense

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

	Year Ended December 31,		
	2025	2024	2023
Cost of sales	$ 2	$ 1	$ 1
Research and development	84	87	75
Selling, general and administrative	67	70	59
Total stock-based compensation expense	$ 153	$ 158	$ 135

Stock-based compensation of $2 million, $3 million, and $2 million was capitalized into inventory for the years ended December 31, 2025, 2024, and 2023, respectively. Capitalized stock-based compensation is recognized as cost of sales when the related product is sold.

As of December 31, 2025, the total unrecognized compensation expense related to unvested equity awards, net of estimated forfeitures, was $232 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,		
	2025	2024	2023
Expected term (years)	6	6	6
Expected volatility	53%	55%	55%
Risk-free interest rate	4.1%	4.2%	4.2%
Expected dividend rate	0.0%	0.0%	0.0%

13. Defined Contribution Plan

The Company sponsors a retirement plan in which substantially all of its full-time employees in the U.S. and certain other foreign countries are eligible to participate. Eligible participants may contribute a percentage of their annual compensation to this plan, subject to statutory limitations. The Company recorded $10 million, $10 million, and $10 million as expense related to the plan for the years ended December 31, 2025, 2024, and 2023, respectively.

14. Income Taxes

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

	Year Ended December 31,		
	2025	2024	2023
Domestic	$ 565	$ 563	$ 609
Foreign	6	4	—
Total loss before income taxes	$ 571	$ 567	$ 609

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

	Year Ended December 31,		
	2025	2024	2023
Current provision for income taxes:			
Federal	$ —	$ —	$ —
State	—	—	(3)
International	4	3	3
Total current tax provision	4	3	—
Deferred tax provision:			
Federal	—	—	—
State	—	—	(2)
International	—	(1)	—
Total deferred tax benefit	—	(1)	(2)
Total provision for (benefit from) income taxes	$ 4	$ 2	$ (2)

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.

For the year ended December 31, 2023, the Company recognized an income tax benefit of $5 million attributable to modifications in its state apportionment methodology, offset by an income tax expense of $3 million from foreign jurisdictions. For the year ended December 31, 2024, the Company recognized income tax expense of $1 million from foreign jurisdictions alongside a nominal amount of state tax. For the year ended December 31, 2025, the Company recognized income tax expense of $4 million from foreign jurisdictions and a nominal amount of state tax. The Company realized no benefit for current year losses due to a full valuation allowance against the U.S. net deferred tax assets.

The table below provides the updated requirements of ASU 2023-09 for the year ended December 31, 2025.

The effective tax rate of our provision for income taxes differs from the federal statutory rate as follows (in millions except percentage amounts):

	Year Ended December 31,	
	2025	
Federal statutory income tax rate	$ (120)	21.0 %
State income taxes, net of federal benefit [1]	—	—
Foreign tax effects	5	(0.9)
Effect of changes in tax laws or rates enacted in the current period	—	—
Effect of cross-border tax laws	5	(0.9)
Tax credits	—	—
Research tax credit	(12)	2.1
Orphan drug credit	(32)	5.6
Change in valuation allowance	145	(25.4)
Nontaxable or nondeductible items		
Share-based payment awards	14	(2.5)
Other	(1)	0.3
Uncertain tax positions	—	—
Other Adjustments	—	—
Provision for income taxes	$ 4	(0.7) %

(1) Includes a nominal amount of state tax. Illinois State tax made up the majority (greater than 50 percent) of the tax effect in this category.

As previously disclosed for the years ended December 31, 2024 and 2023, prior to the adoption of ASU 2023-09, the effective income tax rate differs from the statutory federal income tax rate as follows:

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

Income taxes paid (net of refunds) for the year ended December 31, 2025 is disaggregated as follows (in millions):

	Year Ended December 31,
	2025
Federal income taxes paid (net of refunds)	$ —
State income taxes paid (net of refunds)	—
Foreign income taxes paid (net of refunds)	
Brazil	1
Mexico	1
Other [1]	2
Total income taxes paid (net of refunds)	$ 4

(1) There was a nominal amount of foreign taxes paid (net of refunds) to Canada, Switzerland, France, Japan, and the Netherlands.

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

	Year Ended December 31,	
	2025	2024
Deferred tax assets:		
Loss carryforwards	$ 511	$ 309
Tax credits	426	370
Stock options	46	52
Accruals and reserves	34	32
Fixed assets and intangibles	26	32
Liabilities for sales of future royalties	276	197
Basis difference in equity investments	8	9
Capitalized research and development costs	34	212
Other	—	1
Gross deferred tax assets	1,361	1,214
Valuation allowance	(1,355)	(1,207)
Total deferred tax assets	6	7
Deferred tax liabilities:		
In-process research and development	(30)	(30)
Right-of-use lease assets	(5)	(6)
Gross deferred tax liabilities	(35)	(36)
Net deferred tax liabilities	$ (29)	$ (29)

As of December 31, 2025 and 2024, the Company had approximately $2,104 million and $1,191 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, 2025 and 2024, the Company had approximately $936 million and $744 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, 2025 and 2024, the Company had federal research tax credit carryforwards of approximately $60 million and $45 million, respectively, available to reduce future tax liabilities that will begin to expire in 2031. As of December 31, 2025 and 2024, the Company had state research credit carryforwards of $110 million and $92 million, respectively, available to reduce future tax liabilities. The majority of these credits will be carried forward indefinitely, and others will expire at various dates in the future.

As of December 31, 2025 and 2024, the Company had federal Orphan Drug Credits of approximately $379 million and $339 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, $4 million of federal net operating loss carryforwards, $4 million of state net operating loss carryforwards, and a nominal amount 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 $148 million and $171 million during the years ended December 31, 2025 and 2024, respectively.

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

	December 31,		
	2025	2024	2023
Balance at beginning of year	$ 97	$ 80	$ 67
Additions based on tax positions related to current year	15	15	12
Additions for tax positions of prior years	—	2	1
Reductions for tax positions of prior years	(1)	—	—
Balance at end of year	$ 111	$ 97	$ 80

Approximately $1 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, 2025, 2024 and 2023, the Company recognized nominal amounts for accrued interest and penalties as a component of income tax expense. 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, 2025, the Company had not made a provision for any incremental foreign withholding taxes on approximately $17 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, 2025 remain subject to examination.

15. Commitments and Contingencies

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

Manufacturing and service contract obligations primarily relate to manufacturing of product for our clinical stage pipeline, the majority of which are due in the next 12 months.

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

See "Note 9. Leases" for lease commitments.

Contingencies

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.

16. 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 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. A total of $1 million has been recorded as research and development expense for this agreement to date. There are no further obligations under this agreement.

17. Net Loss per Share

The following table sets forth the computation of the basic and diluted net loss per share during the years ended December 31, 2025, 2024, and 2023 (in millions, except per share data):

	Year Ended December 31,		
	2025	2024	2023
Numerator:			
Net loss	$ (575)	$ (569)	$ (607)
Denominator:			
Weighted-average shares used to compute net loss per share, basic and diluted	98.6	90.5	73.5
Net loss per share, basic and diluted	$ (5.83)	$ (6.29)	$ (8.25)

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 (in millions):

	Year Ended December 31,		
	2025	2024	2023
Options to purchase common stock, restricted stock units, and performance stock units	16.8	16.3	14.2

18. Accumulated Other Comprehensive Income (Loss)

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

	Year Ended December 31,	
	2025	2024
Cumulative foreign currency translation adjustment	$ 1	$ (2)
Unrealized gain on securities available-for-sale	—	1
Total accumulated other comprehensive income (loss)	$ 1	$ (1)

19. Subsequent Events

In February 2026, the Company's Board of Directors approved a strategic restructuring plan that includes a reduction of approximately 10% of the Company's workforce, or the Restructuring Plan. As a result of this reduction in force, the Company estimates that it will incur restructuring charges of approximately $50 million in total in connection with employee related termination and severance costs, charges for the termination of UX143 manufacturing agreements, and other related activities, substantially all of which are expected to be recognized during the first half of 2026. Cash payments related to these costs are expected to be made over the same period.

The Restructuring Plan is intended to reduce the Company's headcount and expenses by focusing resources on the Company's largest value drivers. Management's estimates are based on information available as of the approval date of the Restructuring Plan and are subject to change as the plan is implemented.