ULTRAGENYX PHARMACEUTICAL INC.

FORM 10-Q
(Quarterly Report)

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Address	60 LEVERONI COURT NOVATO, CA, 94949
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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

(Mark One)

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.**

For the quarterly period ended March 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)

Not Applicable
(Former Name, Former Address and Former Fiscal Year, if Changed Since Last Report)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, $0.001 par value	**RARE**	**The Nasdaq Global Select Market**

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES ☑ NO ☐

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or 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 is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☑

As of May 1, 2025, the registrant had 94,542,035 shares of common stock issued and outstanding.

ULTRAGENYX PHARMACEUTICAL INC.

FORM 10-Q FOR THE QUARTER ENDED MARCH 31, 2025

INDEX

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q, or the Quarterly 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 Quarterly Report are forward-looking statements. In some cases, you can identify forward-looking statements by words such as "aim," “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “forecast,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would,” or the negative of these words, or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our commercialization, marketing, and manufacturing capabilities and strategy;
- our expectations regarding the timing of clinical study commencements and reporting results from same;
- the timing and likelihood of regulatory approvals for, or commercialization of, our product candidates;
- the anticipated indications for our product candidates, if approved;
- the potential market opportunities for commercializing our products and product candidates;
- our expectations regarding the potential market size and the size of the patient populations for our products and product candidates, if approved for commercial use;
- estimates of our expenses, revenue, capital requirements, and our needs for additional financing;
- our ability to develop, acquire, and advance product candidates into, and successfully complete, clinical studies;
- the implementation of our business model and strategic plans for our business, products and product candidates and the integration and performance of any businesses we have acquired or may acquire;
- the initiation, timing, progress, and results of ongoing and future preclinical and clinical studies, and our research and development programs;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our products and product candidates;
- our ability to maintain and establish collaborations or strategic relationships or obtain additional funding;
- our ability to maintain and establish relationships with third parties, such as contract research organizations, contract manufacturing organizations, suppliers, and distributors;
- our financial performance, including our expectations for profitability for 2027, and the expansion of our organization;
- our ability to obtain supply of our products and product candidates;
- the scalability and commercial viability of our manufacturing methods and processes;
- developments and projections relating to our competitors and our industry;
- stagnating or worsening business and economic conditions and increasing geopolitical instability, including inflationary pressures, general economic slowdown or a recession, high interest rates, foreign exchange rate volatility, financial institution instability, 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 II, Item 1A. Risk Factors.

Any forward-looking statements in this Quarterly 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 II, Item 1A. Risk Factors and elsewhere in this Quarterly 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 Quarterly 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.

PART I. FINANCIAL INFORMATION

Item 1. ***Financial Statements***

ULTRAGENYX PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(Unaudited)
(In thousands, except share amounts)

	March 31, 2025	December 31, 2024
ASSETS		
Current assets:		
Cash and cash equivalents[(1)]	$ 127,055	$ 173,729
Marketable debt securities	367,385	436,296
Accounts receivable, net	98,839	121,801
Inventory	46,031	45,007
Prepaid expenses and other assets	59,845	40,290
Total current assets	699,155	817,123
Property, plant, and equipment, net	260,906	265,929
Marketable debt securities	68,563	135,004
Intangible assets, net	176,524	178,314
Goodwill	44,406	44,406
Other assets	62,373	62,680
Total assets	$ 1,311,927	$ 1,503,456
LIABILITIES, NONCONTROLLING INTEREST AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 47,450	$ 38,756
Accrued liabilities	173,007	240,973
Lease liabilities	10,487	10,297
Liabilities for sales of future royalties	57,376	49,847
Other liabilities	3,348	4,280
Total current liabilities	291,668	344,153
Lease liabilities	27,786	30,042
Deferred tax liabilities	30,058	30,058
Liabilities for sales of future royalties	794,046	819,824
Other liabilities	17,123	17,082
Total liabilities	1,160,681	1,241,159
Noncontrolling interest	7,000	7,000
Stockholders' equity:		
Preferred stock, par value of $0.001 per share—25,000,000 shares authorized; nil outstanding in 2025 and in 2024	—	—
Common stock, par value of $0.001 per share—250,000,000 shares authorized; outstanding—93,903,785 in 2025 and 92,484,330 in 2024	94	92
Treasury stock, at cost, 162,344 in 2025 and 69,757 in 2024	(7,566)	(3,593)
Deferred compensation obligation	7,566	3,593
Additional paid-in capital	4,252,417	4,212,692
Accumulated other comprehensive loss	(341)	(643)
Accumulated deficit	(4,107,924)	(3,956,844)
Total stockholders' equity	144,246	255,297
Total liabilities, noncontrolling interest and stockholders' equity	$ 1,311,927	$ 1,503,456

(1) The Company's Condensed Consolidated Balance Sheet as of March 31, 2025 and December 31, 2024, includes $12.4 million and $13.5 million, respectively, in cash and cash equivalents that can be used only to settle obligations of the consolidated variable interest entity. See Note 6.

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(Unaudited)
(In thousands, except share and per share amounts)

	Three Months Ended March 31,	
	2025	2024
Revenues:		
Product sales	$ 91,507	$ 62,489
Royalty revenue	47,785	46,344
Total revenues	139,292	108,833
Operating expenses:		
Cost of sales	28,662	17,533
Research and development	165,772	178,487
Selling, general and administrative	87,797	78,160
Total operating expenses	282,231	274,180
Loss from operations	(142,939)	(165,347)
Interest income	6,831	8,824
Change in fair value of equity investments	(157)	3,746
Non-cash interest expense on liabilities for sales of future royalties	(14,342)	(15,847)
Other income (expense)	837	(1,605)
Loss before income taxes	(149,770)	(170,229)
Provision for income taxes	(1,310)	(455)
Net loss	$ (151,080)	$ (170,684)
Net loss per share, basic and diluted	$ (1.57)	$ (2.03)
Shares used in computing net loss per share, basic and diluted	96,288,650	84,286,292

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(Unaudited)
(In thousands)

	Three Months Ended March 31,	
	2025	2024
Net loss	$ (151,080)	$ (170,684)
Other comprehensive income (loss):		
Foreign currency translation adjustments	392	129
Unrealized loss on available-for-sale debt securities	(90)	(1,207)
Other comprehensive income (loss):	302	(1,078)
Total comprehensive loss	$ (150,778)	$ (171,762)

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(Unaudited)
(In thousands, except share amounts)

	Common Stock		Additional Paid-In	Accumulated Other Comprehensive Income (Loss)	Accumulated	Treasury	Deferred Compensation	Total Stockholders'
	Shares	Amount	Capital		Deficit	Stock	Obligation	Equity
Balance as of December 31, 2024	92,484,330	$ 92	$ 4,212,692	$ (643)	$ (3,956,844)	$ (3,593)	$ 3,593	$ 255,297
Stock-based compensation	—	—	39,570	—	—	—	—	39,570
Issuance of common stock under equity plan awards, net of tax	1,419,455	2	155	—	—	—	—	157
Deferred compensation	—	—	—	—	—	(3,973)	3,973	—
Other comprehensive income	—	—	—	302	—	—	—	302
Net loss	—	—	—	—	(151,080)	—	—	(151,080)
Balance as of March 31, 2025	93,903,785	$ 94	$ 4,252,417	$ (341)	$ (4,107,924)	$ (7,566)	$ 7,566	$ 144,246
Balance as of December 31, 2023	82,315,590	$ 82	$ 3,662,346	$ 647	$ (3,387,661)	$ (432)	$ 432	$ 275,414
Stock-based compensation	—	—	36,671	—	—	—	—	36,671
Issuance of common stock under equity plan awards, net of tax	778,447	1	(60)	—	—	—	—	(59)
Deferred compensation	—	—	—	—	—	(2,900)	2,900	-
Other comprehensive loss	—	—	—	(1,078)	—	—	—	(1,078)
Net loss	—	—	—	—	(170,684)	—	—	(170,684)
Balance as of March 31, 2024	83,094,037	$ 83	$ 3,698,957	$ (431)	$ (3,558,345)	$ (3,332)	$ 3,332	$ 140,264

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(Unaudited)
(In thousands)

	Three Months Ended March 31,	
	2025	2024
Operating activities:		
Net loss	$ (151,080)	$ (170,684)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	39,917	36,926
Amortization of discount on marketable debt securities, net	(1,733)	(3,756)
Depreciation and amortization	8,990	8,845
Change in fair value of equity investments	157	(3,746)
Non-cash royalty revenue	(19,187)	(18,063)
Non-cash interest expense on liabilities for sales of future royalties	14,342	15,847
Other	(1,248)	(77)
Changes in operating assets and liabilities:		
Accounts receivable	10,062	(24,908)
Inventory	(763)	(2,124)
Prepaid expenses and other assets	(17,478)	6,553
Accounts payable, accrued, and other liabilities	(48,454)	(35,540)
Net cash used in operating activities	(166,475)	(190,727)
Investing activities:		
Purchase of property, plant, and equipment	(1,324)	(3,211)
Purchase of marketable debt securities	—	(21,928)
Proceeds from sale of marketable debt securities	92	2,845
Proceeds from maturities of marketable debt securities	136,902	128,794
Payments for intangible asset	(15,000)	(10,000)
Other	(780)	(2,065)
Net cash provided by investing activities	119,890	94,435
Financing activities:		
Proceeds from the issuance of common stock under equity plan awards, net of tax	157	(58)
Net cash provided by (used in) financing activities	157	(58)
Effect of exchange rate changes on cash	1,448	(679)
Net decrease in cash, cash equivalents and restricted cash	(44,980)	(97,029)
Cash, cash equivalents and restricted cash at beginning of period	184,159	219,399
Cash, cash equivalents and restricted cash at end of period	$ 139,179	$ 122,370
Supplemental disclosures of non-cash information:		
Stock-based compensation capitalized into ending inventory	$ 2,999	$ 2,786
Costs of property, plant and equipment included in accounts payable, accrued, and other liabilities	$ 1,566	$ 1,280

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

Notes to Condensed Consolidated Financial Statements

1. Organization

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;
- DTX301 is an AAV8 gene therapy product candidate in development for the treatment of patients with ornithine transcarbamylase, or OTC deficiency, the most common urea cycle disorder;
- UX143 (setrusumab), which is subject to the Company's collaboration agreement with Mereo BioPharma 3, or Mereo, is a fully human monoclonal antibody that inhibits sclerostin, a protein that acts on a key bone-signaling pathway and inhibits the activity of bone-forming cells for the treatment of patients with Osteogenesis Imperfecta, or OI;
- GTX-102 is an antisense oligonucleotide, or ASO for the treatment of Angelman syndrome, a debilitating and rare neurogenetic disorder caused by loss-of-function of the maternally inherited allele of the UBE3A gene; and
- UX701 is an adeno-associated virus 9, or AAV9, gene therapy designed to deliver stable expression of a truncated version of the ATP7B copper transporter following a single intravenous infusion to improve copper distribution and excretion from the body and reverse pathological findings of Wilson liver disease.

The Company has sustained operating losses and expects such annual losses to continue in the near term. The Company's ultimate success depends on the outcome of its research and development and commercialization activities. Through March 31, 2025, the Company has relied primarily on its sale of equity securities, its revenues from commercial products, its sale of future royalties, and strategic collaboration arrangements to finance its operations. The Company may need to raise additional capital to fully implement its business plans through the issuance of equity, borrowings, or strategic alliances with partner companies. However, if such financing is not available at adequate levels, the Company would need to reevaluate its operating plans.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying unaudited Condensed 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.

The financial statements have been prepared in accordance with U.S. generally accepted accounting principles, or GAAP, for interim financial information and in accordance with the instructions to Form 10-Q and Rule 10-01 of Regulation S-X. Accordingly, they do not include all of the information and footnotes required by GAAP for complete financial statements. The unaudited interim

Condensed Consolidated Financial Statements have been prepared on the same basis as the annual financial statements. In the opinion of management, the accompanying unaudited Condensed Consolidated Financial Statements reflect all adjustments (consisting only of normal recurring adjustments) considered necessary for a fair presentation. All intercompany accounts and transactions have been eliminated. These financial statements should be read in conjunction with the audited financial statements and notes thereto for the preceding fiscal year contained in the Company's Annual Report on Form 10-K filed on February 19, 2025, or Annual Report, with the United States Securities and Exchange Commission, or the SEC.

The results of operations for the three months ended March 31, 2025 are not necessarily indicative of the results to be expected for the year ending December 31, 2025. The Condensed Consolidated Balance Sheet as of December 31, 2024 has been derived from audited financial statements at that date, but does not include all of the information required by GAAP for complete financial statements.

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 Condensed Consolidated Financial Statements have been prepared in accordance with GAAP. The preparation of the Condensed 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 Condensed 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

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 Condensed Consolidated Balance Sheets that sum to the total of the same such amounts shown in the Condensed Consolidated Statement of Cash Flows (in thousands):

	March 31,	
	2025	2024
Cash and cash equivalents	$ 127,055	$ 112,250
Restricted cash included in other current assets	8,477	6,304
Restricted cash included in other non-current assets	3,647	3,816
Total cash, cash equivalents, and restricted cash shown in the statements of cash flows	$ 139,179	$ 122,370

Credit Losses

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 three months ended March 31, 2025 and 2024.

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 8. Liabilities for Sales of Future Royalties." The Company recorded the liabilities at inception based upon estimated future cash flows discounted at a market rate. The liabilities are being amortized using the effective interest method over the estimated life of the applicable arrangement. In order to determine the amortization of the liabilities, the Company is required to estimate the total amount of future royalty payments to be received by the Company and paid to RPI and OMERS, subject to the capped amount, over the life of the arrangements. The excess of future estimated royalty payments (subject to the capped amount) to RPI and OMERS is recorded as non-cash interest expense over the life of the arrangements. Consequently, the Company estimates an imputed interest on the unamortized portion of the liabilities and records interest expense relating to the transactions.

The Company periodically assesses the expected royalty payments using a combination of historical results, internal projections and forecasts from external sources. To the extent such payments are greater or less than the Company's initial estimates or the timing of such payments is materially different than its original estimates, the Company employs the prospective method to adjust the amortization of the liabilities and the effective interest rate.

Revenue Recognition

Product Sales

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

Provisions for returns and other adjustments are provided for in the period the related revenue is recorded, as estimated by management. These reserves are based on estimates of the amounts earned or to be claimed on the related sales and are reviewed periodically and adjusted as necessary. The Company's estimates of government mandated rebates, chargebacks, estimated product returns, and other deductions depends on the identification of key customer contract terms and conditions, as well as estimates of sales volumes to different classes of payors. If actual results vary, the Company may need to adjust these estimates, which could have a material effect on earnings in the period of the adjustment.

Collaboration, License, and Royalty Revenue

The Company has certain license and collaboration agreements that are within the scope of ASC 808, *Collaborative Agreements*, which provides guidance on the presentation and disclosure of collaborative arrangements. Generally, the classification of the transactions under the collaborative arrangements is determined based on the nature of contractual terms of the arrangement, along with the nature of the operations of the participants. The Company records its share of collaboration revenue, net of transfer pricing related to net sales in the period in which such sales occur, if the Company is considered as an agent in the arrangement. The Company is considered an agent when the collaboration partner controls the product before transfer to the customers and has the ability to direct the use of and obtain substantially all of the remaining benefits from the product. Funding received related to research and development services and commercialization costs is generally classified as a reduction of research

and development expenses and selling, general and administrative expenses, respectively, in the Condensed 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 8. Liabilities for Sales of Future Royalties", for certain royalty payments from net sales of Crysvita in applicable territories that were sold to RPI and OMERS, the Company records the royalty revenue on a prospective basis as non-cash royalty revenue in the Condensed 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.

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, with the option to apply them retrospectively. ASU 2023-09 is effective for fiscal years beginning after December 15, 2024. The Company is currently evaluating the impact of adopting ASU 2023-09.

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

3. Financial Instruments

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 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 thousands):

	March 31, 2025			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 64,245	$ —	$ —	$ 64,245
Time deposits	—	10,000	—	10,000
Corporate bonds	—	325,902	—	325,902
Asset-backed securities	—	51	—	51
U.S. Government Treasury and agency securities	—	109,995	—	109,995
Investment in Solid common stock	1,932	—	—	1,932
Deferred compensation assets	—	16,416	—	16,416
Total financial assets	$ 66,177	$ 462,364	$ —	$ 528,541
Financial Liabilities:				
Deferred compensation liabilities	$ —	$ 16,813	$ —	$ 16,813

	December 31, 2024			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 113,894	$ —	$ —	$ 113,894
Time deposits	—	10,000	—	10,000
Corporate bonds	—	391,731	—	391,731
Commercial paper	—	21,194	—	21,194
Asset-backed securities	—	143	—	143
U.S. Government Treasury and agency securities	—	158,814	—	158,814
Investment in Solid common stock	2,089	—	—	2,089
Deferred compensation assets	—	15,337	—	15,337
Total financial assets	$ 115,983	$ 597,219	$ —	$ 713,202
Financial Liabilities:				
Deferred compensation liabilities	$ —	$ 15,756	$ —	$ 15,756

4. Balance Sheet Components

Cash Equivalents and Marketable Debt Securities

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

	March 31, 2025			
		Gross Unrealized		
	Amortized Cost	Gains	Losses	Estimated Fair Value
Money market funds	$ 64,245	$ —	$ —	$ 64,245
Certificates of deposit and time deposits	10,000	—	—	10,000
Corporate bonds	325,210	734	(42)	325,902
Asset-backed securities	51	—	—	51
U.S. Government Treasury and agency securities	109,770	225	—	109,995
Total	$ 509,276	$ 959	$ (42)	$ 510,193

	December 31, 2024			
		Gross Unrealized		
	Amortized Cost	Gains	Losses	Estimated Fair Value
Money market funds	$ 113,894	$ —	$ —	$ 113,894
Time deposits	10,000	—	—	10,000
Corporate bonds	391,124	809	(202)	391,731
Commercial paper	21,194	—	—	21,194
Asset-backed securities	143	—	—	143
U.S. Government Treasury and agency securities	158,414	404	(4)	158,814
Total	$ 694,769	$ 1,213	$ (206)	$ 695,776

At March 31, 2025, the remaining contractual maturities of available-for-sale securities were less than three years. There have been no significant realized gains or losses on available-for-sale securities for the periods presented. All marketable debt securities with unrealized losses at March 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 thousands):

	March 31, 2025	December 31, 2024
Work-in-process	$ 22,913	$ 21,967
Finished goods	23,118	23,040
Total inventory	$ 46,031	$ 45,007

Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	March 31, 2025	December 31, 2024
Research and clinical study expenses	$ 15,490	$ 24,437
Payroll and related expenses	58,265	94,021
Revenue related reserves	39,721	33,344
Manufacturing and related expenses	38,981	25,143
Commercial and development milestones	—	45,000
Other	20,550	19,028
Total accrued liabilities	$ 173,007	$ 240,973

5. Revenue

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

	Three Months Ended March 31,	
	2025	2024
Product sales:		
Crysvita	$ 55,080	$ 36,241
Dojolvi	17,009	16,362
Evkeeza	11,031	3,275
Mepsevii	8,387	6,611
Total product sales	91,507	62,489
Crysvita royalty revenue	47,785	46,344
Total revenues	$ 139,292	$ 108,833

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

	Three Months Ended March 31,	
	2025	2024
North America	$ 57,792	$ 57,682
Latin America	54,888	35,178
Europe, Middle East, and Africa	23,327	15,973
Asia-Pacific	3,285	—
Total revenues	$ 139,292	$ 108,833

The Company's largest accounts receivable balance was from a collaboration partner and accounted for 41% and 70% of the total accounts receivable balance as of March 31, 2025 and December 31, 2024, respectively. A separate customer accounted for 17% and 4% of the total accounts receivable balance as of March 31, 2025 and December 31, 2024, respectively.

6. Investment in Amlogenyx. Inc.

In July 2024, the Company contributed certain intellectual property rights to Amlogenyx Inc., or Amlogenyx, a subsidiary of the Company, and received 9.0 million shares of common stock of Amlogenyx. A third-party investor along with one of its affiliated entities, and the Company each contributed $7.0 million to Amlogenyx and in exchange, each received approximately 1.6 million shares of series seed preferred stock of Amlogenyx. The purpose of Amlogenyx is to pursue the application of the Company's novel adeno-associated virus, or AAV, gene therapy to treat beta-amyloid disorders and related neurodegenerative diseases.

Amlogenyx was determined to be a VIE and the Company is the primary beneficiary as it has the power to direct the activities that would most significantly impact the economic performance of Amlogenyx, including the performance of R&D activities relating to its sole product candidate. As the primary beneficiary, the Company has consolidated the financial position, results of operations and cash flows of Amlogenyx in its financial statements and all intercompany balances have been eliminated in consolidation. Upon initial consolidation, the non-controlling interest of the third-party investor was recorded at its estimated fair value of $7.0 million, which is equal to their original investment.

As of March 31, 2025 and December 31, 2024, the Condensed Consolidated Balance Sheets included assets of Amlogenyx of $12.5 million and $13.5 million, and liabilities of Amlogenyx of $0.2 million and $0.1 million, respectively. The assets primarily consisted of cash and cash equivalents which may only be used to settle obligations of Amlogenyx.

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

Changes in the carrying value of noncontrolling interest for the three months ended March 31, 2025 are as follows:

	Noncontrolling Interest
As of December 31, 2023	$ —
Issuance of equity from noncontrolling interest	7,000
As of December 31, 2024	$ 7,000
Changes and adjustments	—
As of March 31, 2025	$ 7,000

7. 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, United Kingdom, and Switzerland, or the European Territory, and the Company has the right to develop and commercialize such products in the field of orphan diseases in Mexico and Central and South America, or Latin America.

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%.

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

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

In July 2022, the Company sold to OMERS its right to receive 30% of the future royalty payments due to the Company based on net sales of Crysvita in the U.S. and Canada, subject to a cap, beginning in April 2023, as further described in "Note 8. Liabilities for Sales of Future Royalties."

Royalty Revenue for Sales in the European Territory

KKC has the commercial responsibility for Crysvita in the European Territory. In December 2019, the Company sold its right to receive royalty payments based on sales in the European Territory to Royalty Pharma, effective January 1, 2020, as further described

in “Note 8. Liabilities for Sales of Future Royalties.” Prior to the Company’s sale of the royalty, the Company received a royalty of up to 10% on net sales in the European Territory, which was recognized as the underlying sales occur. Beginning in 2020, the Company records the royalty revenue as non-cash royalty revenues. The Company records this revenue as royalty revenue.

Total Crysvita revenue was as follows (in thousands):

	Three Months Ended March 31,	
	2025	2024
Product sales	$ 55,080	$ 36,241
Revenue in Profit-Share Territory:		
Royalty revenue	28,597	28,281
Non-cash royalty revenue	12,256	12,121
Total revenue in Profit-Share Territory	40,853	40,402
Non-cash royalty revenue in European Territory	6,932	5,942
Total Crysvita revenue	$ 102,865	$ 82,585

Development Activities

In the field of orphan diseases, except for ongoing studies being conducted by KKC, the Company was the lead party for development activities in the Profit-Share Territory and in the European Territory until the applicable transition date. The Company shared the costs for development activities in the Profit-Share Territory and the European Territory conducted pursuant to the development plan before the applicable transition date equally with KKC. In April 2023, which was the transition date for the Profit-Share Territory, KKC became the lead party and became responsible for the costs of the subsequent development activities. However, the Company will continue to equally share in the costs of the studies with KKC that commenced prior to the applicable transition date.

Collaboration Cost Sharing and Payments

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

	Three Months Ended March 31,	
	2025	2024
Research and development	$ (299)	$ (893)
Selling, general and administrative	(1,342)	(1,262)
Cost of sales	18,705	11,077

Collaboration Receivable and Payable

The Company had accounts receivable from KKC in the amount of $40.8 million and $85.4 million from profit-share revenue and royalties, other receivables of $2.4 million and $1.8 million recorded in other current assets, and accrued liabilities of $18.9 million and $7.1 million from amounts owed for transfer price and royalties as well as commercial and development activity reimbursements, as of March 31, 2025 and December 31, 2024, respectively.

Regeneron

In January 2022, the Company announced a collaboration with Regeneron to commercialize Evkeeza for HoFH outside of the U.S. Pursuant to the terms of the agreement, the Company received the rights to develop, commercialize and distribute the product for HoFH in countries outside of the U.S. The Company paid Regeneron a $30.0 million upfront payment. As of March 31, 2025, the Company has recognized an aggregate of $27.5 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. Going forward, the Company is obligated to pay Regeneron up to an aggregate of $35.5 million of future obligations for additional regulatory and sales milestones, if achieved. The Company may share in certain costs for global trials led by Regeneron. Additionally, the Company pays Regeneron a transfer price fee and royalties on certain revenues.

The collaboration agreement is within the scope of ASC 808 which provides guidance on the presentation and disclosure of collaborative arrangements. As the Company is the principal in sales transactions with the customer, the Company recognizes product sales and cost of sales in the period the related sales occur and the related revenue recognition criteria are met. Under the collaboration agreement, Regeneron supplies the product and charges the Company a transfer price from the low 20% range up to 40% on net sales, which is recognized as cost of sales in the Company's Condensed Consolidated Statement of Operations.

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

	Three Months Ended March 31,	
	2025	2024
Research and development	$ 160	$ 551
Cost of sales	2,758	820

The Company had collaboration payables for this arrangement included in accrued liabilities on the Condensed Consolidated Balance Sheets of $2.5 million and $17.8 million as of March 31, 2025 and December 31, 2024, respectively.

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, United Kingdom, and Switzerland, or the Mereo Territory, where Mereo retains commercial rights. Each party will be responsible for post-marketing commitments in their respective territories and Ultragenyx will be responsible for commercial supply in both the Ultragenyx Territory and Mereo Territory.

Upon the closing of the transactions under the License and Collaboration Agreement with Mereo in January 2021, the Company made a payment of $50.0 million to Mereo. To date, the Company has made payments totaling $9.0 million for regulatory milestones achieved. The Company is obligated to pay Mereo up to $245.0 million in future milestone payments, contingent upon the achievement of certain regulatory and commercial milestones. The Company pays for all global development costs and will pay a tiered double-digit percentage royalties to Mereo on net sales in the Ultragenyx Territory. Mereo will pay the Company a fixed double-digit percentage royalty on net sales in the Mereo Territory. If the Company receives and resells an FDA PRV in connection with a new drug application approval, Mereo is entitled to receive a portion of proceeds from the sale of the PRV or a cash payment from the Company, in the event the Company chooses to retain the PRV.

In December 2024, the Company entered into a manufacturing and supply agreement with Mereo where it is responsible for the supply of setrusumab to Mereo in the Mereo territory. Mereo is responsible 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 three months ended March 31, 2025 and 2024, the Company recorded offsets to research and development expense under this arrangement of $0.7 million and nil, respectively.

The Company had receivables from Mereo in the amount of $1.6 million and $0.9 million, recorded in other current assets and accrued liabilities of $0.1 million and $0.1 million for development activity reimbursements, as of March 31, 2025 and December 31, 2024, respectively.

GeneTx Biotherapeutics LLC

In August 2019, the Company entered into a Program Agreement and a Unitholder Option Agreement with GeneTx Biotherapeutics LLC, or GeneTx, to collaborate on the development of GeneTx's GTX-102, an ASO for the treatment of Angelman syndrome. In July 2022, pursuant to the terms of the Unitholder Option Agreement, as amended, the Company exercised the option to acquire GeneTx and entered into a Unit Purchase Agreement, or the Purchase Agreement, pursuant to which the Company purchased all the outstanding units of GeneTx. During the year ended December 31, 2024, the Company achieved a $30.0 million regulatory milestone upon the initiation of the Phase 3 *Aspire* clinical study for GTX-102. The Company is obligated to pay up to $85.0 million in additional regulatory approval milestones for the achievement of U.S. and EU product approvals, and up to

$75.0 million in commercial milestone payments based on annual worldwide net product sales, contingent upon the achievement of the milestones. The Company will also pay tiered mid- to high single-digit percentage royalties based on licensed product annual net sales. If the Company receives and resells an FDA priority review voucher, or PRV, in connection with a new drug application approval, GeneTx unitholders are entitled to receive a portion of proceeds from the sale or a cash payment from the Company if the Company choses to retain the PRV.

As part of the Company's acquisition of GeneTx, the Company assumed a License Agreement with Texas A&M University, or TAMU. To date, the Company recognized an aggregate of $0.5 million for clinical milestones under the TAMU agreement, and have in aggregate up to $23.0 million of future obligations for various future milestones and a nominal annual license fee that may increase up to a maximum of $2.0 million. The Company will also pay mid-single-digit percentage royalties based on licensed product annual net sales. As of March 31, 2025 and December 31, 2024, the Company had nil and $0.5 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.

Other Arrangements

The Company has also entered into several collaborations and/or licensing arrangements in prior periods. Except as disclosed above, there have been no material changes in these arrangements during the three months ended March 31, 2025 as compared to those disclosed in "Note 9. License and Research Agreements" to the Consolidated Financial Statements in the Annual Report.

Under the financial terms of these arrangements, the Company may be required to make payments upon achievement of developmental, regulatory, and commercial milestones, which could be significant. Future milestone payments, if any, will be reflected in the financial statements upon the occurrence of the contingent event. In addition, the Company may be required to pay royalties on future sales if products related to these arrangements are commercialized. The payment of these amounts, however, is contingent upon the occurrence of various future events, which have a high degree of uncertainty.

As described in the Annual Report, the Company holds an equity interest in Solid in connection with its collaboration arrangement. The changes in the fair value of the Company’s equity investment in the common stock of Solid were as follows (in thousands):

	Common stock
As of December 31, 2023	$ 3,204
Change in fair value	(1,115)
As of December 31, 2024	2,089
Change in fair value	(157)
As of March 31, 2025	$ 1,932

8. Liabilities for Sales of Future Royalties

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

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

Proceeds from these transactions were recorded as liabilities for sales of future royalties on the Condensed Consolidated Balance Sheets. Upon inception of the respective arrangements, the Company recorded $320.0 million and $500.0 million, net of transaction costs of $5.8 million and $9.1 million for RPI and OMERS, respectively. The Company records the royalty revenue arising from the net sales of Crysvita in the applicable territories as royalty revenue in the Condensed Consolidated Statements of

Operations over the term of the arrangements. Royalties earned under the RPI and OMERS arrangements from inception to March 31, 2025 have been $106.2 million and $135.5 million, respectively. The Company's effective annual interest rates were 5.4% and 7.5%, for RPI and OMERS, respectively, as of March 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 thousands):

	Liabilities for Sales of Future Royalties		
	RPI	OMERS	Total
December 31, 2023	$ 376,641	$ 514,926	$ 891,567
Royalty revenue	(25,849)	(59,088)	(84,937)
Non-cash interest expense	23,747	39,294	63,041
December 31, 2024	374,539	495,132	869,671
Royalty revenue	(6,932)	(25,659)	(32,591)
Non-cash interest expense	5,086	9,256	14,342
March 31, 2025	$ 372,693	$ 478,729	$ 851,422

9. Stock-Based Awards

As of March 31, 2025, there were 3,235,021 shares available under the 2023 Incentive Plan, 6,409,256 shares available under the Amended & Restated 2014 Employee Stock Purchase Plan, and 205,258 shares available under the Employment Inducement Plan for the future issuance of equity awards.

The table below sets forth the stock-based compensation expense for the periods presented (in thousands):

	Three Months Ended March 31,	
	2025	2024
Cost of sales	$ 503	$ 416
Research and development	20,806	20,541
Selling, general and administrative	18,601	15,977
Total stock-based compensation expense	$ 39,910	$ 36,934

10. Net Loss Per Share

Basic net loss per share has been computed by dividing the net loss by the weighted-average number of shares of common stock outstanding, pre-funded warrants, and treasury stock for deferred compensation obligations required to be settled in shares of common stock. Diluted net loss per share is calculated by dividing net loss by the weighted-average number of shares of common

stock outstanding, pre-funded warrants, and treasury stock for deferred compensation obligations required to be settled in shares of common stock, and potential dilutive securities outstanding during the period.

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:

	Three Months Ended March 31,	
	2025	2024
Options to purchase common stock, restricted stock units, and performance stock units	16,678,554	15,056,294
Employee stock purchase plan	110,625	110,146
	16,789,179	15,166,440

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 up to $350.0 million, from time to time, in at-the-market, or ATM, offerings through Cowen. As of March 31, 2025, no shares have been sold under this agreement.

12. Related Party Transaction

In July 2022, the Company entered into an agreement with a non-profit foundation in which two members of the Company's board of directors, including the Company's Chief Executive Officer, at the time also served as board members of the foundation, whereby an aggregate $1.0 million contribution is being paid to the foundation over a four-year period, beginning in the third quarter of 2022, to support rare disease education and awareness. As a result, the Company recorded nil and $0.3 million as research and development expense for this agreement for the three months ended March 31, 2025 and 2024, respectively. A total of $0.8 million has been recorded as research and development expense for this agreement to date.

13. Accumulated Other Comprehensive Loss

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

	March 31, 2025	December 31, 2024
Foreign currency translation adjustments	$ (1,258)	$ (1,650)
Unrealized gain on available-for-sale securities	917	1,007
Total accumulated other comprehensive loss	$ (341)	$ (643)

Item 2. ***Management's Discussion and Analysis of Financial Condition and Results of Operations***

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with the accompanying unaudited Condensed Consolidated Financial Statements and related notes in Item 1 and with the audited Consolidated Financial Statements and the related notes included in our Annual Report on Form 10-K for the year ended December 31, 2024, or Annual Report.

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.

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.

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. The following table summarizes our approved products and pipeline of clinical product candidates:

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

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

Approved Products

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

Crysvita is a fully human monoclonal antibody administered via subcutaneous injection, that targets fibroblast growth factor 23, or FGF23, developed for the treatment of XLH. XLH is a rare, hereditary, progressive, and lifelong musculoskeletal disorder characterized by renal phosphate wasting caused by excess FGF23 production. There are approximately 48,000 patients with XLH in the developed world, including approximately 36,000 adults and 12,000 children. Crysvita is the only approved treatment that addresses the underlying cause of XLH. Crysvita is approved in the U.S., the EU and certain other regions for the treatment of XLH in adult and pediatric patients one year of age and older.

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

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

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.

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.

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.

Clinical Product Candidates

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

UX143 (setrusumab) is a fully human monoclonal antibody administered by IV that inhibits sclerostin, a protein that acts on a key bone-signaling pathway by inhibiting the activity of bone-forming cells and promoting bone resorption. Setrusumab is being developed for the treatment of OI, or brittle bone disease, which is caused by variants in the *COL1A1* or *COL1A2* genes, leading to either reduced or abnormal collagen and changes in bone metabolism. There are an estimated 60,000 patients in the developed world affected by OI. UX143 has received orphan drug designation from the U.S. Food and Drug Administration, or FDA, and European Medicines Agency, or EMA, Rare Pediatric Disease designation and Breakthrough Designation from the FDA, and was accepted into the EMA's Priority Medicines, or PRIME, program. Setrusumab is subject to our collaboration agreement with Mereo and is the lead clinical asset in our bone endocrinology franchise.

GTX-102 for the treatment of Angelman Syndrome

GTX-102 is an antisense oligonucleotide, or ASO, administered by intrathecal injection that inhibits expression of the paternal *UBE3A* antisense. GTX-102 is being developed for the treatment of Angelman syndrome, a debilitating and rare neurogenetic disorder caused by loss-of-function of the maternally inherited allele of the *UBE3A* gene. There are an estimated 60,000 patients in the developed world affected by Angelman syndrome. GTX-102 has received Fast Track Designation, Orphan Drug Designation and Rare Pediatric Disease Designation from the FDA and has been accepted into the EMA's PRIME program.

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.

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.

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.

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.

Recent Program Updates

UX143 for the treatment of OI

In January 2025, we announced that the Phase 3 *Orbit* study is progressing to the second interim analysis expected in mid-2025. Patients in the *Cosmic* study also continue to be treated with either setrusumab or IV-BP therapy and will be evaluated in parallel with the second *Orbit* interim analysis in mid-2025. If *Orbit* progresses to full study completion in the fourth quarter of 2025, *Cosmic* will also continue to a data readout, to align with the *Orbit* readout without spending alpha at a mid-year interim assessment.

GTX-102 for the treatment of Angelman Syndrome

We are currently randomizing and dosing patients in *Aspire*, the 48-week Phase 3 study of GTX-102. Approximately 120 patients, between four and 17 years of age, with a genetically confirmed diagnosis of full maternal UBE3A gene deletion will be enrolled and randomized 1:1 to the GTX-102 or sham comparator group. The primary endpoint will be improvement in cognition assessed by Bayley-4 cognitive raw score, and the key secondary endpoint will be the Multi-domain Responder Index (MDRI) across

the five domains of cognition, receptive communication, behavior, gross motor function, and sleep. We expect to complete enrollment for the Phase 3 study in the second half of 2025.

UX111 for the treatment of MPS IIIA

In February 2025, the FDA granted Priority Review to the previously submitted BLA for UX111 with a Prescription Drug User Fee Act, or PDUFA, action date of August 18, 2025.

DTX401 for the treatment of GSDIa

In May 2024, we previously disclosed that the Phase 3 *GlucoGene* study for the treatment of patients aged eight years and older with GSDIa achieved its primary endpoint, demonstrating that treatment with DTX401 resulted in a statistically significant and clinically meaningful reduction in daily cornstarch intake compared with placebo at Week 48. At Week 48, patients entered a 48-week Crossover Period where patients previously treated with placebo were treated with DTX401. In May 2025 we announced data from this Crossover Period, that demonstrated greater reductions in total daily cornstarch were observed in both the ongoing DTX401 group (-60%) with a mean follow-up of 120 weeks and the Crossover Placebo to DTX401 group (-64%) with a mean duration on therapy with DTX401 of 69 weeks. 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 will be included as part of a BLA submission expected in mid-2025.

DTX301 for the treatment of OTC deficiency

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 the percentage of patients who achieve a response as measured by the change in 24-hour plasma ammonia levels and discontinuation or reduction ammonia-scavenger medications and protein-restricted diet. Based on an amended protocol, the change in 24-hour ammonia levels will be measured through Week 36, after which the study would unblind and patients will be followed for a total of up to 64 weeks to determine the complete responders able to move safely to both ammonia-scavenger medications and protein-restricted diet control.

UX701 for the treatment of Wilson disease

In May 2025, we announced enrollment had begun in Cohort 4 of 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). We expect to enroll five patients in Cohort 4 who will receive immunomodulation therapy with rituximab and tacrolimus, in addition to the prophylactic oral corticosteroid regimen patients in Cohorts 1 through 3 received, prior to being dosed with UX701. Enrollment in Cohort 4 is expected to complete in the second half of 2025.

The pivotal, Stage 2 protocol was amended to a 52-week, randomized, open-label, active-controlled design, evaluating the safety and efficacy of UX701 following dose selection in Stage 1. The Stage 2 primary endpoints include comparisons between the UX701 and active control groups of change in 24-hour urinary copper from Baseline at Week 52 and percent reduction in standard of care medication by Week 52.

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 $151.1 million and $170.7million for the three months ended March 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.

Our total revenues were $139.3 million and $108.8 million for the three months ended March 31, 2025 and 2024, respectively. The increase in revenue was largely driven by an increase in demand for our approved products.

As of March 31, 2025, we had $563.0 million in available cash, cash equivalents, and marketable debt securities.

Critical Accounting Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our Condensed Consolidated Financial Statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these Condensed 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. There have been no material changes in our critical accounting policies during the three months ended March 31, 2025, as compared to those disclosed in "Management's Discussion and Analysis of Financial Condition and Results of Operations — Critical Accounting Policies and Significant Judgments and Estimates" in our Annual Report.

Results of Operations

Comparison of the three months ended March 31, 2025 to the three months ended March 31, 2024:

Revenue (dollars in thousands)

	Three Months Ended March 31,		Dollar	%
	2025	2024	Change	Change
Product sales:				
Crysvita	$ 55,080	$ 36,241	$ 18,839	52%
Dojolvi	17,009	16,362	647	4%
Evkeeza	11,031	3,275	7,756	237%
Mepsevii	8,387	6,611	1,776	27%
Total product sales	91,507	62,489	29,018	46%
Crysvita royalty revenue	47,785	46,344	1,441	3%
Total revenues	$ 139,292	$ 108,833	$ 30,459	28%

Our product sales increased by $29.0 million for the three months ended March 31, 2025 compared to the same period in 2024. The increase is primarily due to an increase in demand for Crysvita in Latin America resulting from an increase in the number of patients on therapy, the launch of Evkeeza in Japan and several markets in Europe, Middle East and Africa territories, or EMEA, and the continued increase in demand for our other approved products.

Our Crysvita royalty revenue increased by $1.4 million for the three months ended March 31, 2025 as compared to the same period in 2024.

Cost of Sales (dollars in thousands)

	Three Months Ended March 31,		Dollar	%
	2025	2024	Change	Change
Cost of sales	$ 28,662	$ 17,533	$ 11,129	63%

Cost of sales increased by $11.1 million for the three months ended March 31, 2025, compared to the same period in 2024. The increase in cost of sales was due to an increase in demand for our approved products, primarily Crysvita in Latin America and Evkeeza in EMEA and Japan.

Research and Development Expenses (dollars in thousands)

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

Clinical programs include study conduct and manufacturing costs related to clinical program candidates. Translational research includes costs for preclinical study work and costs related to preclinical programs prior to IND filing. Upfront license, acquisition, and milestone fees include any significant expenses related to strategic licensing agreements. Approved products include costs for disease monitoring programs for post-marketing clinical studies, medical affairs activities to support scientific discovery efforts on existing programs, and regulatory costs for unapproved regions. Infrastructure costs include direct costs related to laboratory, IT, and equipment depreciation costs, and overhead allocations for human resources, IT, and other allocable costs.

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

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

	Three Months Ended March 31,		Dollar	%
	2025	2024	Change	Change
Clinical programs:				
Gene therapy programs				
DTX301	$ 7,829	$ 15,048	$ (7,219)	-48%
DTX401	17,948	18,339	(391)	-2%
UX701	5,737	11,801	(6,064)	-51%
UX111	11,341	6,070	5,271	87%
CMC costs	(442)	1,417	(1,859)	-131%
Total gene therapy programs	42,413	52,675	(10,262)	-19%
Biologic and nucleic acid programs				
GTX102	15,988	11,295	4,693	42%
UX053	—	472	(472)	-100%
UX143	20,312	24,120	(3,808)	-16%
Total biologic and nucleic acid programs	36,300	35,887	413	1%
Translational research	10,176	15,690	(5,514)	-35%
Approved products	8,558	10,028	(1,470)	-15%
Infrastructure	22,947	20,882	2,065	10%
Stock-based compensation	20,806	20,541	265	1%
Other research and development	24,572	22,784	1,788	8%
Total research and development expenses	$ 165,772	$ 178,487	$ (12,715)	-7%

Total research and development expenses decreased by $12.7 million for the three months ended March 31, 2025 compared to the same period in 2024. The decrease in research and development expenses was primarily due to:

- for gene therapy programs, a decrease of $10.3 million, primarily due to the timing of the UX701 manufacturing runs and the recognition of contract manufacturing costs for DTX301 for the three months ended March 31, 2024 which did not recur for the three months ended March 31, 2025, partially offset by an increase in UX111 manufacturing costs in preparation for commercial launch;
- for biologic and nucleic acid programs, an increase of $0.4 million, primarily related to the continued clinical progress of the GTX102 program and associated clinical development and manufacturing expenses, partially offset by a reduction in development expense on UX143;
- for translational research, a decrease of $5.5 million, primarily related to a decrease in manufacturing expense for IND-stage projects;
- for approved products, a decrease of $1.5 million for the three months ended March 31, 2025, primarily due to reduced compassionate use costs for Dojolvi;
- for infrastructure, an increase of $2.1 million, primarily related to the allocation of certain staffing costs; and
- for other research and development expenses, an increase of $1.8 million, primarily related to increased staffing to support internal manufacturing, and administrative and general support.

We expect our annual research and development expenses to moderate in the future as we advance our product candidates through clinical development. The timing and amount of expenses incurred will depend largely upon the outcomes of current or future clinical studies for our product candidates as well as the related regulatory requirements, manufacturing costs, and any costs associated with the advancement of our preclinical programs.

Selling, General and Administrative Expenses (dollars in thousands)

	Three Months Ended March 31,		Dollar	%
	2025	2024	Change	Change
Selling, general and administrative	$ 87,797	$ 78,160	$ 9,637	12%

Selling, general and administrative expenses increased by $9.6 million for the three months ended March 31, 2025 compared to the same period in 2024. The increase was primarily due to higher employee compensation costs as well as the recognition of reimbursement for a cost share arrangement that impacted selling, general and administrative expenses for the three months ended March 31, 2024, which did not recur during the three months ended March 31, 2025.

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

Interest Income (dollars in thousands)

	Three Months Ended March 31,		Dollar	%
	2025	2024	Change	Change
Interest income	$ 6,831	$ 8,824	$ (1,993)	-23%

Interest income decreased by $2.0 million for the three months ended March 31, 2025 compared to the same period in 2024, primarily due to lower marketable debt securities balances.

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

	Three Months Ended March 31,		Dollar	%
	2025	2024	Change	Change
Change in fair value of equity investments	$ (157)	$ 3,746	$ (3,903)	*

* not meaningful

For the three months ended March 31, 2025 and 2024, we recorded a net decrease of $0.2 million and a net increase of $3.7 million, respectively, in the fair value of our equity investments due to unrealized loss and gain, respectively, on our investment in Solid Biosciences Inc., or Solid, common stock.

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

	Three Months Ended March 31,		Dollar	%
	2025	2024	Change	Change
Non-cash interest expense on liabilities for sales of future royalties	$ (14,342)	$ (15,847)	$ 1,505	-9%

The non-cash interest expense on liabilities for sales of future royalties decreased by $1.5 million for the three months ended March 31, 2025, compared to the same period in 2024, primarily due to a reduction in total royalty obligation balances as a result of increased royalties generated from our collaboration partner, KKC. To the extent the royalty payments are greater or less than our initial estimates or the timing of such payments is materially different than our original estimates, we prospectively adjust the effective interest rate.

Other Income (Expense) (dollars in thousands)

	Three Months Ended March 31,		Dollar	%
	2025	2024	Change	Change
Other income (expense)	$ 837	$ (1,605)	$ 2,442	-152%

Other income increased by $2.4 million for the three months ended March 31, 2025, compared to the same period in 2024. These changes were primarily due to fluctuations to our exposures in foreign exchange rates.

Provision for Income Taxes (dollars in thousands)

	Three Months Ended March 31,		Dollar	%
	2025	2024	Change	Change
Provision for income taxes	$ (1,310)	$ (455)	$ (855)	188%

The provision for incomes taxes increased by $0.9 million for the three months ended March 31, 2025, compared to the same period in 2024.

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 March 31, 2025, we had $563.0 million in available cash, cash equivalents, and marketable debt securities. We believe that our existing capital resources will be sufficient to fund our projected operating requirements for at least the next 12 months. Our cash, cash equivalents, and marketable debt securities are held in a variety of deposit accounts, interest-bearing accounts, corporate bond securities, commercial paper, U.S. government securities, asset-backed securities, and money market funds. Cash in excess of immediate requirements is invested with a view toward liquidity and capital preservation, and we seek to minimize the potential effects of concentration and credit risk.

In June 2024, we completed an underwritten public offering for the sale of shares of common stock and pre-funded warrants. The total proceeds that we received from the offering were $381.0 million, net of underwriting discounts and commissions.

In February 2024, we entered into a Sales Agreement with Cowen and Company, LLC, or Cowen, pursuant to which the Company may offer and sell shares of the Company's common stock having an aggregate offering proceeds up to $350.0 million, from time to time, in ATM offerings through Cowen. As of March 31, 2025 no shares have been sold under this agreement.

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

	Three Months Ended March 31,	
	2025	2024
Cash used in operating activities	$ (166,475)	$ (190,727)
Cash provided by investing activities	119,890	94,435
Cash provided by (used in) financing activities	157	(58)
Effect of exchange rate changes on cash	1,448	(679)
Net decrease in cash, cash equivalents and restricted cash	$ (44,980)	$ (97,029)

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 three months ended March 31, 2025 was $166.5 million and primarily reflected a net loss of $151.1 million, partially offset by non-cash items of $41.2 million, net, which consisted primarily of stock-based compensation, amortization of discounts on marketable debt securities, depreciation and amortization, non-cash royalty revenue, and non-cash interest expense related to the sale of future royalties. The change in operating assets and liabilities also reflected a net use of cash of $56.6 million, primarily due to a net decrease in accounts payable, accrued and other liabilities primarily due to the payout of the 2024 annual bonuses and decreases in accrued collaboration for payment of a milestone to a collaboration partner of $30.0 million as well as an increase in prepaid manufacturing expense, partially offset by a decrease in accounts receivable related to timing of orders and collections.

Cash used in operating activities for the three months ended March 31, 2024 was $190.7 million and primarily reflected a net loss of $170.7 million, partially offset by non-cash items of $36.0 million, net, which consisted primarily of stock-based compensation, amortization of discounts on marketable debt securities, the change in fair value of equity investments, depreciation and amortization, non-cash royalty revenue, and non-cash interest expense related to the sale of future royalties. The change in operating assets and liabilities also reflected a net use of cash of $56.0 million, primarily due to an increase in accounts receivable primarily related to an increase in sales of our approved products and timing of when orders were received, partially offset by a net decrease in accounts payable, accrued and other liabilities primarily due to the payout of the 2023 annual bonuses and decreases in accrued collaboration for the payment of a regulatory milestone to a collaboration partner.

Cash Provided by Investing Activities

Cash provided by investing activities for the three months ended March 31, 2025 was $119.9 million and was primarily related to $137.0 million from net activities in marketable debt securities, partially offset by the payment to a collaboration partner of $15.0 million for the achievement of a milestone under the collaboration agreement recorded as an intangible asset.

Cash provided by investing activities for the three months ended March 31, 2024 was $94.4 million and was primarily related to $109.7 million from net activities in marketable debt securities, partially offset by the payment to a collaboration partner of $10.0 million for the achievement of a milestone under the collaboration agreement recorded as an intangible asset.

Cash Provided by (Used in) Financing Activities

Cash provided by financing activities for the three months ended March 31, 2025 was $0.2 million.

Cash used in financing activities for the three months ended March 31, 2024 was $0.1 million.

Funding Requirements

We anticipate that, excluding non-recurring items, we will continue to generate annual losses in the near term as we continue the development of, and seek regulatory approvals for, our product candidates, and continue with commercialization of approved products. We may require additional capital to fund our operations, to complete our ongoing and planned clinical studies, to commercialize our products, to continue investing in early-stage research capabilities to promote our pipeline growth, to continue to acquire or invest in businesses or products that complement or expand our business, including future milestone payments thereunder, and to further develop our general infrastructure and such funding may not be available to us on acceptable terms or at all.

If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may be required to delay, limit, reduce the scope of, or terminate one or more of our clinical studies, research and development programs, future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our future funding requirements will depend on many factors, including the following:

- the scope, rate of progress, results and cost of our clinical studies, nonclinical testing, and other related activities;
- the cost of manufacturing clinical supplies, and establishing commercial supplies, of our product candidates, products that we have begun to commercialize, and any products that we may develop in the future;
- the cost of operating our GMP gene therapy manufacturing facility;

- the number and characteristics of product candidates that we pursue;
- the cost, timing, and outcomes of regulatory interactions and approvals;
- the cost and timing of establishing our commercial infrastructure, and distribution capabilities;
- the impact of macroeconomic conditions, including general economic slowdowns, changing interest rates and inflation on our business operations and operating results; and
- the terms and timing of any collaborative, licensing, marketing, distribution, acquisition and other arrangements that we may establish, including any required upfront milestone, royalty, reimbursements or other payments thereunder.

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

Contractual Obligations and Commitments

Material contractual obligations arising in the normal course of business primarily consist of operating and finance leases and manufacturing and service contract obligations.

Future minimum lease payments under non-cancellable leases as of March 31, 2025, were approximately $46.6 million, of which $13.9 million is due within one year.

Manufacturing and service contract obligations primarily relate to manufacturing of inventory for our approved products. As of March 31, 2025, we had obligations of approximately $97.2 million, of which $84.9 million is due within one year.

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.

Item 3. *Quantitative and Qualitative Disclosures about Market Risk*

Interest Rate Risk

Our exposure to market risk for changes in interest rates relates primarily to interest earned on our cash equivalents and marketable debt securities. The primary objective of our investment activities is to preserve our capital to fund operations. A secondary objective is to maximize income from our investments without assuming significant risk. Our investment policy provides for investments in low-risk, investment-grade debt instruments. As of March 31, 2025, we had cash, cash equivalents, and marketable debt securities totaling $563.0 million, compared to $745.0 million as of December 31, 2024, which included bank deposits, money market funds, U.S. government treasury and agency securities, and investment-grade corporate bond securities which are subject to default, changes in credit rating, and changes in market value. The securities in our investment portfolio are classified as available for sale and are subject to interest rate risk and will decrease in value if market interest rates increase. A hypothetical 100 basis point change in interest rates during any of the periods presented would not have had a material impact on the fair market value of our cash equivalents and marketable debt securities as of March 31, 2025 or December 31, 2024. To date, we have not experienced a loss of principal on any of our investments and as of March 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 macro-economic 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 three months ended March 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 Condensed Consolidated Financial Statements.

Item* 4. *Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Management carried out an evaluation, under the supervision and with the participation of our Principal Executive Officer and Principal Financial Officer, of the effectiveness of our "disclosure controls and procedures" as of the end of the period covered by this Quarterly Report, pursuant to Rules 13a-15(b) and 15d-15(b) under the Securities Exchange Act of 1934, or the Exchange Act. In connection with that evaluation, our Principal Executive Officer and Principal Financial Officer concluded that our disclosure controls and procedures were effective and designed to provide reasonable assurance that the information required to be disclosed is recorded, processed, summarized, and reported within the time periods specified in the SEC rules and forms as of March 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 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.

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 quarter ended March 31, 2025, that has materially affected, or is reasonably likely to materially affect our internal control over financial reporting.

PART II. OTHER INFORMATION

Item 1. *Legal Proceedings*

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

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

Aurobindo and Navinta answered the complaint in December 2024. Esjay filed a motion to dismiss the suit in December 2024. We filed an opposition to Esjay's motion to dismiss in January 2025. In April 2025, Navinta filed a motion for judgment on the pleadings, which we opposed in May 2025.

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

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

Catalent filed its response, which included a motion to dismiss the fraud claim alleged in the suit, in December2024. We filed an amended complaint in reply to Catalent's response in February 2025. Catalent moved to dismiss the amended complaint in March 2025. We filed our opposition to Catalent's motion to dismiss in May 2025.

Except as disclosed above, we are not currently a party to any other material legal proceedings. We may, however, in the ordinary course of business face various claims brought by third parties or government regulators and, from time to time, make claims or take legal actions to assert our rights, including claims relating to our directors, officers, stockholders, intellectual property rights, employment matters and the safety or efficacy of our products. Any of these claims could subject us to costly litigation and, while we generally believe that we have adequate insurance to cover many different types of liabilities, our insurance carriers may deny coverage, may be inadequately capitalized to pay on valid claims, or our policy limits may be inadequate to fully satisfy any damage awards or settlements. If this were to happen, the payment of any such awards could have a material adverse effect on our consolidated operations, cash flows and financial position. Additionally, any such claims, whether or not successful, could damage our reputation and business.

Item 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 Quarterly 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.

The following description of the risk factors associated with our business includes any material changes to and supersedes the description of the risk factors associated with our business previously disclosed in Part I, Item 1A of the Annual Report.

Risk Factor Summary

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

- Our revenue may be adversely affected if the market opportunities for our products and product candidates are smaller than expected.
- Our competitors may develop therapies that are similar, more advanced, or more effective than ours.
- We may not successfully manage expansion of our company.
- Commercial success of our products depends on the degree of market acceptance.
- We face uncertainty related to insurance coverage and reimbursement status of our newly approved products.
- If we, or our third-party partners, are unable to maintain effective proprietary rights for our products or product candidates, we may not be able to compete effectively.
- Claims of intellectual property infringement may prevent or delay our development and commercialization efforts.
- We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.
- We may face competition from biosimilars of our biologics products and product candidates or from generic versions of our small-molecule products and product candidates, which may result in a material decline in sales of affected products.
- We could lose license rights that are important to our business if we fail to comply with our obligations in the agreements under which we license intellectual property and other rights from third parties.
- We may become involved in lawsuits to protect or enforce our patents or the patents of our licensors, or be subject to claims that challenge the inventorship or ownership of our patents.
- Changes to patent laws in the U.S. and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.
- We may not be able to protect our intellectual property rights throughout the world.
- We have limited experience as a company operating our own manufacturing facility.
- Our success depends in part on our ability to retain our President and Chief Executive Officer and other qualified personnel.
- Our revenue may be impacted if we fail to obtain or maintain orphan drug exclusivity for our products.
- Our operating results may be adversely impacted if our intangible assets become impaired.
- We may not be successful in identifying, licensing, developing, or commercializing additional product candidates.
- We may fail to comply with laws and regulations or changes in laws and regulations could adversely affect our business.
- We are exposed to risks related to international expansion of our business outside of the U.S.
- Our employees or consultants may engage in misconduct which could cause significant liability for us.
- If we are found to have promoted off-label uses for our products, we may become subject to significant liability from the FDA and other regulatory agencies.
- Our business may be adversely affected in the event of computer system failures or security breaches.
- We or our third-party partners may be adversely affected by earthquakes or other serious natural disasters.
- We may incur various costs and expenses and risks related to acquisition of companies or products or strategic transactions.
- The market price of our common stock is highly volatile.
- Future sales and issuances of our common stock could dilute the percentage ownership of our current stockholders and result in a decline in stock price.
- Provisions in our amended and restated certificate of incorporation and by-laws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us or could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

- We face general risks related to our ability to maintain effective internal controls over financial reporting, additional tax liabilities related to our operations, our ability to use our net operating loss carryforwards, costs of litigation, stockholder activism and increased scrutiny regarding our ESG practices and disclosures.

Risks Related to Our Financial Condition and Capital Requirements

We have a history of operating losses and expect to continue to incur operating losses in the near term.

Since inception, we have been engaged in substantial research and development and capital investments, and we have operated at an operating loss each year and expect to continue doing so in the near term. While we currently expect to achieve profitability for the year 2027, our expectations are based on a variety of assumptions, and actual results, including whether we achieve profitability on our expected timeline or at all, may materially differ from our expectations. Our operating results, including our ability to achieve profitability, will depend, in part, on non-recurring events, the success of our commercialization efforts, and the rate of our future expenditures. We anticipate that our expenses will increase substantially if and as we:

- continue our research and nonclinical and clinical development of our product candidates;
- expand the scope of our current clinical studies for our product candidates;
- advance our programs into more expensive clinical studies;
- initiate additional nonclinical, clinical, or other studies for our product candidates;
- pursue preclinical and clinical development for additional indications for existing products and product candidates;
- change or add additional manufacturers or suppliers;
- expand upon our manufacturing-related facilities and capabilities, particularly as we continue to increase operations at our GMP gene therapy manufacturing facility;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical studies;
- continue to establish Medical Affairs field teams to initiate relevant disease education;
- continue to establish or grow a marketing and distribution infrastructure and field force to commercialize our products and any product candidates for which we may obtain marketing approval;
- continue to manage our international subsidiaries and establish new ones;
- continue to operate as a public company and comply with legal, accounting and other regulatory requirements;
- seek to identify, assess, license, acquire, and/or develop other product candidates, technologies, and/or businesses;
- make milestone or other payments under any license or other agreements;
- seek to maintain, protect, and expand our intellectual property portfolio;
- seek to attract and retain skilled personnel;
- create additional infrastructure, including facilities and systems, to support the growth of our operations, our product development, and our commercialization efforts; and
- experience any delays or encounter issues with any of the above, including, but not limited to, failed studies, complex results, safety issues, inspection outcomes, or other regulatory challenges that require longer follow-up of existing studies, additional major studies, or additional supportive studies in order to pursue marketing approval.

Even if we do achieve profitability, we may not be able to sustain or increase such profitability on a quarterly or yearly basis. Our operating results may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

We have limited experience in generating revenue from product sales.

Our ability to generate significant revenue from product sales depends on our ability, alone or with strategic collaboration partners, to successfully commercialize our products and to complete the development of, and obtain the regulatory and marketing approvals necessary to commercialize, our product candidates. Our ability to generate substantial future revenue from product sales, including named patient sales, depends heavily on our success in many areas, including, but not limited to:

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

If the number of our addressable rare disease patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice, or treatment guidelines, or any other reasons, we may not generate significant revenue from sales of our products, even if they receive regulatory approval.

We may need to raise additional capital to fund our activities. Such additional financing may not be available on acceptable terms, if at all. Failure to obtain this necessary capital when needed may force us to delay, limit, or terminate our product development efforts or other activities.

As of March 31, 2025, our available cash, cash equivalents, and marketable debt securities were $563.0 million. We may need additional capital to continue to commercialize our products, and to develop, obtain regulatory approval for, and to commercialize, all of our product candidates. In addition, our operating plans may change as a result of many factors that may currently be unknown to us, and we may need to seek additional funds sooner than planned. Our future funding requirements will depend on many factors, including but not limited to:

- the scope, rate of progress, results, and cost of our clinical studies, nonclinical testing, and other related activities;
- the cost of manufacturing clinical and commercial supplies of our products and product candidates;
- the cost of creating additional infrastructure, including facilities and systems, such as systems in our GMP gene therapy manufacturing facility;
- the cost of operating and maintaining our gene therapy manufacturing facility;
- the number and characteristics of the product candidates that we pursue;
- the cost, timing, and outcomes of regulatory approvals;
- the cost and timing of establishing and operating our international subsidiaries;
- the cost and timing of establishing and operating field forces, marketing, and distribution capabilities;

- the cost and timing of other activities needed to commercialize our products; and
- the terms and timing of any collaborative, licensing, acquisition, and other arrangements that we may establish, including any required milestone, royalty, and reimbursements or other payments thereunder.

Any additional fundraising efforts may divert our management's attention from their day-to-day activities, which can adversely affect our ability to develop our product candidates and commercialize our products. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all, particularly in light of the current macroeconomic conditions, including changing interest rates, inflation and market instability arising from increasing political and trade tensions. The terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities by us, whether equity or debt, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. If we incur debt, it could result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell, or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. We have in the past sought and may in the future seek funds through a sale of future royalty payments similar to our transactions with Royalty Pharma and OMERS or through collaborative partnerships, strategic alliances, and licensing or other arrangements, such as our transaction with Daiichi Sankyo Co., Ltd., or Daiichi Sankyo, and we may be required to relinquish rights to some of our technologies or product candidates, future revenue streams, research programs, and other product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results, and prospects. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.

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

If our cash flows are materially and adversely affected or if we are unable to access our existing cash, cash equivalents and investments and/or are unable to obtain funding on a timely basis, or at all, we may be required to significantly curtail, delay, or discontinue one or more of our research or development programs or the commercialization of our products and any approved product candidates or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition, and results of operations.

Risks Related to the Discovery and Development of Our Product Candidates

Clinical drug development involves a lengthy, complex, and expensive process with uncertain outcomes and the potential for substantial delays, and the results of earlier studies may not be predictive of future study results.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive, complex, time consuming, and uncertain as to outcome. We cannot guarantee that any clinical studies will be conducted as planned or completed on schedule, if at all. We have also had difficulties in recruiting clinical site investigators and clinical staff for our studies, and may continue to experience such difficulties. Additionally, a failure of one or more clinical studies can occur at any stage of testing, and our future clinical studies may not be successful. Product candidates that have shown promising results in early-stage clinical studies may still suffer significant setbacks or fail in subsequent clinical studies. The safety or efficacy results generated to date in clinical studies do not ensure that later clinical studies will demonstrate similar results. Further, we have reported and expect to continue to report preliminary or interim data from our clinical trials. Preliminary or interim data from our clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and/or more patient data become available. Such data may show initial evidence of clinical benefit, but as patients continue to be assessed and more patient data become available, there is a risk that any therapeutic effects are no longer durable in patients and/or decrease over time or cease entirely. As a result, preliminary or interim data should be considered carefully and with caution until the final data are available. Results from investigator-sponsored studies or compassionate-use studies may not be confirmed in company-sponsored studies or may negatively impact the prospects for our programs. Additionally, given the nature of the rare diseases we are seeking to treat, we often devise newly-defined endpoints to be tested in our studies, which can lead to subjectivity in interpreting study results and could result in regulatory agencies not agreeing with the validity of our endpoints, or our interpretation of the clinical data, and therefore delaying or denying approval. Given the illness of the patients in our studies and the nature of their rare diseases, we have also been required to, or have chosen to, conduct certain studies on an open-label basis. We have in the past, and may in the future, elect to review interim clinical data at multiple time points during the studies, which could introduce bias into the study results and potentially result in denial of approval.

In the biopharmaceutical industry, there is a high failure rate for drugs and biologics proceeding through clinical studies, and product candidates in later stages of clinical studies may fail to show the desired safety and efficacy despite having progressed through nonclinical studies and initial clinical studies. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical studies due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies.

Scenarios that can prevent successful or timely completion of clinical development include but are not limited to:

- delays or failures in generating sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation or continuation of human clinical studies or filings for regulatory approval;
- failure to demonstrate a starting dose for our product candidates in the clinic that might be reasonably expected to result in a clinical benefit;
- delays or failures in developing gene therapy, or other novel and complex product candidates, which are expensive and difficult to develop and manufacture;
- delays resulting from a shutdown, or uncertainty surrounding the potential for future shutdowns of the U.S. government, including the FDA;
- delays or failures in reaching a consensus with regulatory agencies on study design;
- delays in reaching agreement on acceptable terms with contract research organizations, or CROs, clinical study sites, and other clinical trial-related vendors;
- failure or delays in obtaining required regulatory agency approval and/or IRB or EC approval at each clinical study site or in certain countries;
- failure to correctly design clinical studies which may result in those studies failing to meet their endpoints or the expectations of regulatory agencies;
- changes in clinical study design or development strategy resulting in delays related to obtaining approvals from IRBs or ECs and/or regulatory agencies to proceed with clinical studies;
- imposition of a clinical hold by regulatory agencies after review of an IND application or amendment, another equivalent application or amendment, or an inspection of our clinical study operations or study sites;
- delays in recruiting suitable patients to participate in our clinical studies;
- difficulty collaborating with patient groups and investigators;
- failure by our CROs, other third parties, or us to adhere to clinical study requirements;
- failure to perform in accordance with the FDA's and/or ICH's good clinical practices requirements or applicable regulatory guidelines in other countries;
- delays in patients' completion of studies or their returns for post-treatment follow-up;
- patients dropping out of a study;
- adverse events associated with the product candidate occurring that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- greater than anticipated costs associated with clinical studies of our drug candidates, including as a result of inflation;
- clinical studies of our drug candidates producing negative or inconclusive results, which may result in us deciding, or regulators requiring us, to conduct additional clinical or nonclinical studies or to abandon drug development programs;
- competing clinical studies of potential alternative product candidates or investigator-sponsored studies of our product candidates; and
- delays in manufacturing, testing, releasing, validating, or importing/exporting sufficient stable quantities of our product candidates for use in clinical studies or the inability to do any of the foregoing.

Any inability to successfully complete nonclinical and clinical development could result in additional costs to us or negatively impact our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional toxicology, comparability or other studies to bridge our modified product candidates to earlier versions. Clinical study delays could also shorten any periods during which our products have commercial exclusivity and may allow our competitors to bring products to market before we do, which could negatively impact our ability to obtain orphan exclusivity and to successfully commercialize our product candidates and may harm our business and results of operations.

If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our products may be delayed and the credibility of our management may be adversely affected and, as a result, our stock price may decline.

For planning purposes, we estimate the timing of the accomplishment of various scientific, clinical, regulatory, and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials, the timing of patient dosing, the timing, type or clarity of data from clinical trials, the submission or acceptance of regulatory filings, and the potential approval of such regulatory filings. We periodically make public announcements about the expected timing of some of these milestones. All of these milestones are based on a variety of assumptions, but the actual timing of these milestones can vary dramatically from our estimates. If we do not meet these publicly announced milestones, the commercialization of our products may be delayed and the credibility of our management may be adversely affected and, as a result, our stock price may decline.

We may find it difficult to identify and enroll patients in our clinical studies due to a variety of factors, including the limited number of patients who have the diseases for which our product candidates are being studied and other unforeseen events. Difficulty in enrolling patients could delay or prevent clinical studies of our product candidates.

Identifying and qualifying patients to participate in clinical studies of our product candidates is critical to our success. The timing of our clinical studies depends in part on the speed at which we can recruit patients to participate in testing our product candidates, and we may experience delays in our clinical studies if we encounter difficulties in enrollment.

Each of the conditions for which we plan to evaluate our current product candidates is a rare genetic disease. Accordingly, there are limited patient pools from which to draw for clinical studies. For example, we estimate that approximately 6,000 patients worldwide suffer from GSDIa, for which DTX401 is being studied, and these all may not be treatable if they are immune to the AAV viral vector.

In addition to the rarity of these diseases, the eligibility criteria of our clinical studies will further limit the pool of available study participants as we will require patients to have specific characteristics that we can measure or to assure their disease is either severe enough or not too advanced to include them in a study. The process of finding and diagnosing patients is costly and time-consuming, especially since the rare diseases we are studying are commonly underdiagnosed. We also may not be able to identify, recruit, and enroll a sufficient number of appropriate patients to complete our clinical studies because of demographic criteria for prospective patients, the perceived risks and benefits of the product candidate under study, the proximity and availability of clinical study sites for prospective patients, and the patient referral practices of physicians. The availability and efficacy of competing therapies and clinical studies can also adversely impact enrollment. If patients are unwilling to participate in our studies for any reason (such as drug-related side effects), the timeline for and our success in recruiting patients, conducting studies, and obtaining regulatory approval of potential products may be delayed or impaired, the commercial prospects of our product candidates will be harmed, and our ability to generate product sales from any of these product candidates could be delayed or prevented. Delays in completing our clinical studies will increase our costs, slow down our product candidate development and approval process, and jeopardize our ability to commence product sales and generate revenue.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming, and inherently unpredictable. Even if we achieve positive results in our pre-clinical and clinical studies, if we are ultimately unable to obtain timely regulatory approval for our product candidates, our business will be substantially harmed.

Our future success is dependent on our ability to successfully commercialize our products and develop, obtain regulatory approval for, and then successfully commercialize one or more product candidates. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities. We have only obtained regulatory approval for three products that we have developed, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval. Further, as the clinical trial requirements of regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the product candidates, the regulatory approval process for novel product candidates, such as our gene therapy product candidates, can be more expensive and take longer than for other product candidates, leading to fewer product approvals. To date, very few gene therapy products have received regulatory approval in the U.S. or Europe. The regulatory framework and oversight over development of gene therapy products has evolved and may continue to evolve in the future. Within the FDA, the Center for Biologics Evaluation and Research, or CBER, regulates gene therapy products. Within the CBER, the review of gene therapy and related products is consolidated in the Office of Cellular, Tissue and Gene Therapies, and the FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its reviews. The CBER works closely with the National Institutes of Health, or NIH. The FDA and the NIH have published guidance with respect to the development and submission of gene therapy protocols. For example, in January 2020, the FDA issued final guidance to set forth the framework for the development, review and approval of gene therapies. The final guidance pertains to the development of gene therapies for the treatment of specific disease categories, including rare diseases, and to manufacturing and long-term follow up issues relevant to gene therapy, among other topics. At the same time the FDA issued guidance describing the FDA's approach for determining whether two gene therapy products were the same or different for the purpose of assessing orphan drug exclusivity. Within the European Medicines Agency, or EMA, special rules apply to gene therapy and related products as they are considered advanced therapy medicinal products, or ATMPs. Pursuant to the ATMP Regulation, the Committee on Advanced Therapies, or CAT, is responsible in conjunction with the Committee for Medicinal Products for Human Use, or CHMP, for the evaluation of ATMPs. The CHMP and CAT are also responsible for providing guidelines on ATMPs. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs and include, among other things, the preclinical studies required to characterize ATMPs. The manufacturing and control information that should be submitted in a MAA; and post-approval measures required to monitor patients and evaluate the long-term efficacy and potential adverse reactions of ATMPs. Although such guidelines are not legally binding, compliance with them is often necessary to gain and maintain approval for product candidates. In addition to the mandatory risk-management plan, or RMP, the holder of a marketing authorization for an ATMP must put in place and maintain a system to ensure that each individual product and its starting and raw materials, including all substances coming into contact with the cells or tissues it may contain, can be traced through the sourcing, manufacturing, packaging, storage, transport, and delivery to the relevant healthcare institution where the product is used.

To obtain regulatory approval in the U.S. and other jurisdictions, we must comply with numerous and varying requirements regarding safety, efficacy, chemistry, manufacturing and controls, clinical studies (including good clinical practices), commercial sales, pricing, and distribution of our product candidates, as described in "Item 1. Business – Government Regulation" of our 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. On January 20, 2025, the U.S. President signed an executive order creating an advisory commission, the "Department of Government Efficiency" to reform federal government processes and reduce expenditures. 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. 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:

- regulatory authorities may disagree with the design, implementation, or conduct of our clinical studies;
- regulatory authorities may change their guidance or requirements for a development program for a product candidate;

- the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- regulatory authorities may disagree with our interpretation of data from nonclinical studies or clinical studies;
- the data collected from clinical studies of our product candidates may not be sufficient to support the submission of an NDA, or biologics license application, or BLA, or other submission or to obtain regulatory approval;
- we may be unable to demonstrate to regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities used to manufacture our clinical and commercial supplies;
- the U.S. government may be shut down, which could delay the FDA;
- failure of our nonclinical or clinical development to comply with an agreed upon Pediatric Investigational Plan, or PIP, which details the designs and completion timelines for nonclinical and clinical studies and is a condition of marketing authorization in the EU; and
- the approval policies or regulations of regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Furthermore, the disease states we are evaluating often do not have clear regulatory paths for approval and/or do not have validated outcome measures. In these circumstances, we work closely with the regulatory authorities to define the approval path and may have to qualify outcome measures as part of our development programs. Additionally, many of the disease states we are targeting are highly heterogeneous in nature, which may impact our ability to determine the treatment benefit of our potential therapies.

This lengthy and uncertain approval process, as well as the unpredictability of the clinical and nonclinical studies, may result in our failure to obtain regulatory approval to market any of our product candidates, or delayed regulatory approval.

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

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

The FDA Rare Pediatric Disease Priority Review Voucher Program, or PRV Voucher Program, awards Priority Review Vouchers, or PRVs, to sponsors of rare pediatric product applications that meet certain criteria. Under the program, a company that receives an approval for a product for a rare pediatric disease (as determined by the applicable regulations) may qualify for a PRV that can be redeemed to receive Priority Review of a subsequent marketing application for a different product. PRVs may also be sold by the company to third parties. We received PRVs under the PRV Voucher Program in connection with the approval of Mepsevii and Crysvita in 2018 and subsequently sold these two PRVs to third parties for an average amount of $105.3 million for each PRV. The PRV Voucher Program began to sunset on December 20, 2024 such that the FDA may only award a PRV for a product application if a company received the rare pediatric disease designation from the FDA for the product candidate by December 20, 2024 and the FDA will cease awarding PRVs after September 30, 2026. Renewal of the PRV Voucher Program is subject to approval by Congress and it is currently uncertain whether the program will be renewed and whether any such renewal will be retroactively effective. If the PRV program is not renewed by Congress and our qualifying product candidates are approved by the FDA after the deadline of September 30, 2026, we will not be eligible to receive additional PRVs for our product candidates and accordingly, we would be unable to use such PRV for Priority Review for another one of our programs or to sell such PRV, which sale has the potential to generate significant proceeds.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay, or halt clinical studies or further development, and could result in a more restrictive label, the delay or denial of regulatory approval by the FDA or other comparable foreign authorities, or a Risk Evaluation and Mitigation Strategy, or REMS, plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, restricted distribution, a communication plan for healthcare providers, and/or other elements to assure safe use. Our product candidates are in development and the safety profile has not been established. Further, as one of the goals of Phase 1 and/or Phase 2 clinical trials is to identify the highest dose of treatment that can be safely provided to study participants, adverse side effects, including serious adverse effects, have occurred in certain studies as a result of changes to the dosing regimen during such studies and may occur in future studies. Results of our studies or investigator-sponsored trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our studies could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny or withdraw approval of our product candidates for any or all targeted indications.

Additionally, notwithstanding our prior or future regulatory approvals for our product candidates, if we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the product's label or restrict the product's approved use;
- we may be required to create a REMS plan;
- we may be required to change the way the product is administered;
- patients and physicians may elect not to use our products, or reimbursement authorities may elect not to reimburse for them; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved.

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

Gene therapy remains a novel technology. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. For example, certain gene therapy trials using AAV8 vectors (although at significantly higher doses than those used in our gene therapy product candidates) and other vectors led to several well-publicized adverse events, including cases of leukemia and death. The risk of cancer or death remains a concern for gene therapy and there can be no assurance that it will not occur in any of our planned or future clinical studies. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. Serious adverse events in our clinical trials, or

other clinical trials involving gene therapy products, particularly AAV gene therapy products such as candidates based on the same capsid serotypes as our product candidates, or occurring during use of our competitors' products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity, could result in increased government regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our gene therapy product candidates, stricter labeling requirements for those gene therapy product candidates that are approved and a decrease in demand for any such gene therapy product candidates.

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

The manufacturing process used to produce our gene therapy product candidates is novel, complex, and has not been validated for commercial use. Several factors could cause production interruptions, including equipment malfunctions, malfunctions of internal information technology systems, regulatory inspections, facility contamination, raw material shortages or contamination, natural disasters, geopolitical instability, disruption in utility services, human error or disruptions in the operations of our suppliers. Further, given that cGMP gene therapy manufacturing is a nascent industry, there are a small number of CMOs with the experience necessary to manufacture our gene therapy product candidates and we may have difficulty finding or maintaining relationships with such CMOs or hiring experts for internal manufacturing and accordingly, our production capacity may be limited.

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

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

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

Our products and any product candidates that are approved in the future remain subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, distribution, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the U.S. and requirements of comparable foreign regulatory authorities, as described in "Item 1. Business – Government Regulation" of our Annual Report.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA, and comparable foreign regulatory authority, requirements, including ensuring that quality control and manufacturing procedures conform to Good Manufacturing Practices, or GMP, regulations. As such, we and our contract manufacturers are subject to continual review and inspection to assess compliance with GMP and adherence to commitments made in any NDA, BLA, MAA, or other comparable application for approval in another jurisdiction. Although we are not involved in the day-to-day operations of our contract manufacturers, we are ultimately responsible for ensuring that our products are manufactured in accordance with GMP regulations. Regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our products, product candidates or the associated quality systems for compliance with the regulations applicable to the activities being conducted. Due to the complexity of the processes used to manufacture our products and product candidates, we or any of our collaborators or contract manufacturers may be unable to comply with GMP regulations in a cost-effective manner and may be unable to initially or continue to pass a federal, national or international regulatory inspection. If we, our collaborators, such as KKC or Regeneron, or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA or other applicable regulatory authority can impose regulatory sanctions including, among other things, warning or untitled letters, fines, unanticipated compliance expenses, the temporary or permanent suspension of a clinical study or commercial sales, recalls or seizures of product or the temporary or permanent closure

of a facility or withdrawal of product approval, enforcement actions and criminal or civil prosecution. If supply from one approved manufacturer is interrupted due to failure to maintain regulatory compliance, an alternative manufacturer would need to be qualified through an NDA or BLA supplement or MAA variation, or equivalent foreign regulatory filing, which could result in delays in product supply. The regulatory agencies may also require additional studies if a new manufacturer, material, testing method or standard is relied upon for commercial production. Switching manufacturers, materials, test methods or standards may involve substantial costs and may result in a delay in our desired clinical and commercial timelines. Accordingly, we and others with whom we work are required continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or other conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical studies, and surveillance to monitor the safety and efficacy of the product candidate. We could also be asked to conduct post-marketing clinical studies to verify the safety and efficacy of our products in general or in specific patient subsets. If original marketing approval was obtained via the accelerated approval or conditional marketing authorization pathways, we would be required to conduct a successful post-marketing clinical study to confirm clinical benefit for our products. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval. We will be required to report certain adverse events and manufacturing problems, if any, to the FDA and comparable foreign regulatory authorities. The holder of an approved NDA, BLA, MAA, or other comparable application must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process.

If we fail to comply with applicable regulatory requirements, or there are safety or efficacy problems with a product, a regulatory agency or enforcement authority may, among other things:

- issue warning or notice of violation letters;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approval;
- suspend any of our ongoing clinical studies;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities;
- seize or detain products, or require a product recall; or
- require entry into a consent decree.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

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

We face an inherent risk of product liability exposure related to the testing of our approved products and product candidates in human clinical trials, as well as in connection with commercialization of our current and future products. If we cannot successfully defend ourselves against claims that any of our approved products or product candidates caused injuries, we could incur substantial liabilities. There can be no assurance that our product liability insurance, which provides coverage in the amount of $15.0 million in the aggregate, will be sufficient in light of our current or planned clinical programs. We may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability, or losses may exceed the amount of insurance that we carry. A product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business. In addition, regardless of merit or eventual outcome, product liability claims may result in impairment of our business reputation, withdrawal of clinical study participants, costs due to related litigation, distraction of management's attention from our primary business, initiation of investigations by regulators, substantial monetary awards to patients or other claimants, the inability to commercialize our product candidates, and decreased demand for our product candidates, if approved for commercial sale.

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

We are developing companion diagnostic tests to identify the right patients for certain of our product candidates and to monitor response to treatment. In certain cases, diagnostic tests may need to be developed as companion diagnostics and regulatory approval obtained in order to commercialize some product candidates. We currently use and expect to continue to use biomarkers to identify the right patients for certain of our product candidates. We may also need to develop predictive biomarkers in the future. We can offer no assurances that any current or future potential biomarker will in fact prove predictive, be reliably measured, or be accepted as a measure of efficacy by the FDA or other regulatory authorities. In addition, our success may depend, in part, on the development and commercialization of companion diagnostics. We also expect the FDA will require the development and regulatory approval of a companion diagnostic assay as a condition to approval of our gene therapy product candidates. There has been limited success to date industrywide in developing and commercializing these types of companion diagnostics. Development and manufacturing of companion diagnostics is complex and there are limited manufacturers with the necessary expertise and capability. Even if we are able to successfully develop companion diagnostics, we may not be able to manufacture the companion diagnostics at a cost or in quantities or on timelines necessary for use with our product candidates. To be successful, we need to address a number of scientific, technical and logistical challenges. We are currently working with a third party to develop companion diagnostics, however, we have little experience in the development and commercialization of diagnostics and may not ultimately be successful in developing and commercializing appropriate diagnostics to pair with any of our product candidates that receive marketing approval. We rely on third parties for the automation, characterization and validation, of our bioanalytical assays, companion diagnostics and the manufacture of critical reagents.

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

Risks Related to our Reliance on Third Parties

We rely on third parties to conduct our nonclinical and clinical studies and perform other tasks for us. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or comply with regulatory requirements, we may be exposed to sub-optimal quality and reputational harm, we may not be able to obtain regulatory approval for or commercialize our product candidates, and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third parties, including CROs, collaborative partners, and independent investigators to analyze, collect, monitor, and manage data for our ongoing nonclinical and clinical programs. We rely on third parties for execution of our nonclinical and clinical studies, and for estimates regarding costs and efforts completed, and we control only certain aspects of their activities. We and our CROs and other vendors and partners are required to comply with GMP, GCP, and GLP, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, and comparable foreign regulatory authorities for all of our product candidates in development. Regulatory authorities enforce these regulations through periodic inspections of study sponsors, principal investigators, study sites, and other contractors. If we or any of our CROs or other vendors and partners, including the sites at which clinical studies are conducted, fail to comply with applicable regulations, the data generated in our nonclinical and clinical studies may be deemed unreliable and the FDA, EMA, or comparable foreign regulatory authorities may deny approval and/or require us to perform additional nonclinical and clinical studies before approving our marketing applications, which would delay the approval process. We cannot make assurances that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical studies comply with GCP regulations or that nonclinical studies comply with GLP regulations. In addition, our clinical studies must be conducted with products produced under GMP regulations. If the regulatory authorities determine that we have failed to comply with GLP, GMP, or GCP regulations, they may deny approval of our product candidates and/or we may be required to repeat clinical or nonclinical studies, which would delay the regulatory approval process.

Our CROs and other vendors and partners are not our employees, and we cannot control whether or not they devote sufficient time and resources to our on-going nonclinical and clinical programs, except for the limited remedies available to us under our agreements with such third parties. If our vendors and partners do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements, or for other reasons, our clinical studies may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. CROs and other vendors and partners have also generated higher costs than anticipated as a result of changes in scope of work or otherwise. As a result, the commercial prospects for our product candidates could be harmed, our costs could increase, and our ability to generate revenue could be delayed.

If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative vendors or do so on commercially reasonable terms. Switching or adding additional vendors involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new vendor commences work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. Our efforts to manage our relationships with our vendors and partners can provide no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition, and business prospects.

We also rely on third parties in other ways, including efforts to support patient diagnosis and identify patients, to assist our finance and legal departments, and to provide other resources for our business. Use of these third parties could expose us to sub-optimal quality, missed deadlines, and non-compliance with applicable laws, all of which could result in reputational harm to us and negatively affect our business.

We are dependent on KKC for the commercialization of Crysvita in our markets, including the U.S. and Canada, and for our supply of Crysvita in our markets. Failure by KKC to commercialize Crysvita in those markets, or to supply Crysvita to us, could result in a material adverse effect on our business and operating results.

Pursuant to the terms of our collaboration and license agreement with KKC, or the collaboration agreement, commercialization responsibilities for Crysvita in the U.S. and Canada transitioned from us to KKC in April 2023. KKC also has the sole right to commercialize Crysvita in Europe and, at certain specified times, in 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 in countries where it has the sole right to commercialize the product candidates that limit commercialization efforts in those countries or in countries where we have the right to commercialize our product candidates;
- KKC may make decisions regarding market access and pricing in countries where it has the sole right to commercialize our product candidates which can negatively impact our commercialization efforts in countries where we have the right to commercialize our product candidates;
- KKC may fail to manufacture or supply sufficient drug product of Crysvita in compliance with applicable laws and regulations or otherwise for our development and clinical use or commercial use, which could result in program delays or lost revenue;
- KKC may elect to develop and commercialize Crysvita indications with a larger market than XLH and at a lower price, thereby reducing the profit margin on sales of Crysvita for any orphan indications, including XLH;
- if KKC were to breach or terminate the agreement with us, we would no longer have any rights to develop or commercialize Crysvita or such rights would be limited to non-terminated countries;
- KKC may terminate its agreement with us, adversely affecting our potential revenue from licensed products; and
- the timing and amounts of expense reimbursement that we may receive are uncertain, and the total expenses for which we are obligated to reimburse KKC may be greater than anticipated.

We rely on third parties to manufacture our products and our product candidates and we are subject to a multitude of manufacturing risks, any of which could substantially increase our costs and limit the supply of our products and product candidates.

As we currently lack the resources and the full capability to manufacture all of our products and product candidates on a clinical or commercial scale, we rely on third parties to manufacture, store and distribute our products and product candidates. Although we oversee the contract manufacturers, we cannot control the manufacturing process of, and are substantially dependent on, our contract manufacturing partners for compliance with the regulatory requirements. See the risk factor above entitled "- *Even if we obtain regulatory approval for our product candidates, our products remain subject to regulatory scrutiny."* Further, we depend on our manufacturers to purchase from third-party suppliers the materials necessary to produce our products and product candidates. There are a limited number of suppliers for raw materials that we use to manufacture our drugs, placebos, or active controls, and there may be a need to identify alternate suppliers to prevent or mitigate a possible disruption of the manufacture of the materials necessary to produce our products and product candidates for our clinical studies, and, if approved, ultimately for commercial sale. We also do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. We may also experience interruptions in supply of product if the product or raw material components fail to meet our quality control standards or the quality control standards of our suppliers.

Further, manufacturers that produce our products and product candidates may not have experience producing our products and product candidates at commercial levels and may not produce our products and product candidates at the cost, quality, quantities, locations, and timing needed to support profitable commercialization. We have not yet secured manufacturing capabilities for commercial quantities of all of our product candidates and may be unable to negotiate binding agreements with manufacturers to support our commercialization activities on commercially reasonable terms. Even if our third-party product manufacturers develop acceptable manufacturing processes that provide the necessary quantities of our products and product candidates in a compliant and timely manner, the cost to us for the supply of our products and product candidates manufactured by such third parties may be high and could limit our profitability. For instance, KKC is our sole supplier of commercial quantities of Crysvita. The supply price to us for commercial sales of Crysvita in Latin America is 30% of net sales, which is higher than the typical cost of sales for companies focused on rare diseases.

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

- The process of manufacturing our products and product candidates is extremely susceptible to product loss due to contamination, equipment failure or improper installation or operation of equipment, or vendor or operator error. Even minor deviations from normal manufacturing processes for our products and any of our product candidates could result in reduced production yields, product defects, and other supply disruptions. If microbial, viral, or other contaminations are discovered in our products and product candidates or in the manufacturing facilities in which our products and product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination.
- The manufacturing facilities in which our products and product candidates are made could be adversely affected by equipment failures, labor shortages, raw material shortages, natural disasters, power failures, actual or threatened public health emergencies, and numerous other factors.

Any adverse developments affecting manufacturing operations for our products and product candidates may result in shipment delays, inventory shortages, lot failures, withdrawals or recalls, or other interruptions in the supply of our products and product candidates. Due to their stage of development, small volume requirements, and infrequency of batch production runs, we carry limited amounts of safety stock for our products and product candidates. We have, and may in the future, be required to take inventory write-offs and incur other charges and expenses for products and product candidates that fail to meet specifications, undertake costly remediation efforts, or seek more costly manufacturing alternatives.

The drug substance and drug product for our products and most of our product candidates are currently acquired from single-source suppliers. The loss of these suppliers, or their failure to supply us with the necessary drug substance or drug product, could materially and adversely affect our business.

We acquire most of the drug substances and drug products for our products and product candidates from single sources. If any single source supplier breaches an agreement with us, or terminates the agreement in response to an alleged breach by us, ceases operations, is acquired, enters into exclusive arrangements with a competitor or otherwise becomes unable or unwilling to fulfill its supply obligations, we would not be able to manufacture and distribute the product or product candidate until a qualified alternative supplier is identified, which could significantly impair our ability to commercialize such product or delay the development of such product candidate. For example, the drug substance and drug product for Crysvita and Evkeeza are made, respectively, by KKC pursuant to a license and collaboration agreement and supply agreements and Regeneron pursuant to a supply agreement. Further, single source suppliers are also used for our gene therapy programs and for Dojolvi, for which we are in the process of qualifying our alternative supplier. We cannot provide assurances that qualifying alternate sources, if available at all, for any of our drug substances and drug products, and establishing relationships with such sources would not result in significant expense, supply disruptions or delay in the commercialization of our products or the development of our product candidates. Additionally, we may not be able to enter into supply arrangements with an alternative supplier on commercially reasonable terms or at all. The terms of any new agreement may also be less favorable or more costly than the terms we have with our current supplier. A delay in the commercialization of our products or the development of our product candidates or having to enter into a new agreement with a different third-party on less favorable terms than we have with our current suppliers could have a material adverse impact upon on our business. Furthermore, geopolitical tensions with China including the Congressional legislative proposal, titled the BIOSECURE Act, which would, among other things, prohibit U.S. federal funding in connection with biotechnology equipment or services produced or provided by Chinese biotechnology companies, and the recent requests by certain Congressional leaders that WuXi AppTech Co. and its affiliates be added to certain U.S. Government restricted entity lists, could lead to our competitors and other companies moving to suppliers outside of China, including to our current suppliers. Significant increases in business at our single source suppliers resulting from such activities could adversely limit capacity at such suppliers to manufacture our products or result in price increases, interruptions or delays of our products.

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

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

Risks Related to Commercialization of Our Products and Product Candidates

If the market opportunities for our products and product candidates are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer. Because the target patient populations of our products and product candidates are small, and the addressable patient population potentially even smaller, we must be able to successfully identify patients and acquire a significant market share to achieve profitability and growth.

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

We have competitors both in the U.S. and internationally, including major multinational pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, startups, academic research institutions, government agencies, and public and private research institutions. Many of our competitors have substantially greater financial, technical, and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries can often result in even more resources being concentrated in our competitors. As a result, these companies may obtain regulatory approval more rapidly than we are able to and may be more effective in selling and marketing their products as well. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring, or licensing on an exclusive basis, products that are more effective or less costly than any product candidate that we may develop, or achieve earlier patent protection, regulatory approval, product commercialization, and market penetration than we do. Additionally, technologies developed by our competitors may render our potential products and product candidates uneconomical or obsolete, and we may not be successful in marketing our products and product candidates against competitors. Moreover, we also face increased competition from other companies that are using AI, some of whom may be able to more quickly and effectively identify and develop novel drug candidates compared to us and our business partners, which could impair our ability to compete effectively and have a material adverse effect on our business, results of operations, or financial condition.

We may not be able to effectively manage the expansion of our organization, including building an integrated commercial organization. If we are unable to expand our existing commercial infrastructure or enter into agreements with third parties to market and sell our products and product candidates, as needed, we may be unable to increase our revenue.

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

expand our commercial team in the United States as well as in Europe, Latin America and the Asia-Pacific region. This infrastructure consists of both office-based as well as field teams with technical expertise, and is expected to be expanded as we approach the potential approval dates of additional products that result from our development programs. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees, and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenue could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

We, as a company, have limited, experience selling and marketing our product and only some of our employees have prior experience promoting other similar products while employed at other companies. As we increase the number and range of our commercialized products, we may experience additional complexities in our sales process and strategy and may encounter difficulties in allocating sufficient resources to sales and marketing of certain products. Further, as we launch additional products or as demand for our products change, our initial estimate of the size of the required field force may be materially more or less than the size of the field force actually required to effectively commercialize our product candidates. As such, we may be required to hire larger teams to adequately support the commercialization of our products and product candidates or we may incur excess costs in an effort to optimize the hiring of commercial personnel. With respect to certain geographical markets, we may enter into collaborations with other entities to utilize their local marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If our future collaborators do not commit sufficient resources to commercialize our future products, if any, and we are unable to develop the necessary marketing capabilities on our own, we will be unable to generate sufficient product sales to sustain our business. We face competition from companies that currently have extensive and well-funded marketing and sales operations. Without a large internal team or the support of a third party to perform key commercial functions, we may be unable to compete successfully against these more established companies.

The commercial success of any current or future product will depend upon the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community.

Even with the requisite approvals from the FDA and comparable foreign regulatory authorities, the commercial success of our current and future products will depend in part on the medical community, patients, and payors accepting our current and future products as medically useful, cost-effective, and safe. Any product that we bring to the market may not gain market acceptance by physicians, patients, payors, and others in the medical community. The degree of market acceptance of any of our current and future products will depend on a number of factors, including:

- the efficacy of the product as demonstrated in clinical studies and potential advantages over competing treatments;
- the prevalence and severity of any side effects, including any limitations or warnings contained in a product's approved labeling;
- the clinical indications for which approval is granted;
- relative convenience and ease of administration;
- the cost of treatment, particularly in relation to competing treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the effectiveness of our field forces and marketing efforts;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party insurance coverage and reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in nonclinical and clinical studies, market acceptance of the product will not be fully known until after it is launched. Our efforts to educate the medical community and payors on the benefits of the product candidates require significant resources and may never be successful. If our current and future products fail to achieve an adequate level of acceptance by physicians, patients, payors, and others in the medical community, we will not be able to generate sufficient revenue to become or remain profitable.

The insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue.

Our target patient populations are small, and accordingly the pricing, coverage, and reimbursement of our products and product candidates, if approved, must be adequate to support our commercial infrastructure. Our per-patient prices must be sufficient to recover our development and manufacturing costs and potentially achieve profitability. We expect the cost of a single administration of gene therapy products, such as those we are developing, to be substantial, when and if they achieve regulatory approval. Accordingly, the availability and adequacy of coverage and reimbursement by governmental and private payors are essential for most patients to afford expensive treatments such as ours, assuming approval. Sales of our products and product candidates, if approved, will depend substantially, both domestically and abroad, on the extent to which their costs will be paid for by health maintenance, managed care, pharmacy benefit, and similar healthcare management organizations, or reimbursed by government authorities, private health insurers, and other payors. If coverage and reimbursement are not available, are available only to limited levels, or are not available on a timely basis, we may not be able to successfully commercialize our products and product candidates, if approved. For example, deteriorating economic conditions and political instability in certain Latin American countries and in 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 U.S. Department of Health and Human Services, decides whether and to what extent a new drug will be covered and reimbursed under Medicare. Private payors tend to follow the coverage reimbursement policies established by CMS to a substantial degree. It is difficult to predict what CMS or private payors will decide with respect to reimbursement for products such as ours, especially our gene therapy product candidates as there is a limited body of established practices and precedents for gene therapy products.

Outside the U.S., international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries will put pressure on the pricing and usage of our products and product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medicinal products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in foreign markets, the reimbursement for our products may be reduced compared with the U.S. and may be insufficient to generate commercially reasonable revenue and profits. The timing to complete the negotiation process in each country is highly uncertain, and in some countries outside of the U.S., we expect the process to exceed several months. Even if a price can be negotiated, countries frequently request or require reductions to the price and other concessions over time, including retrospective “clawback” price reductions. Additionally, member states of the EU have regularly imposed new or additional cost containment measures for pharmaceuticals such as volume discounts, cost caps, clawbacks and free products for a portion of the expected therapy period. For example, in France, we estimate clawback reserves on Dojolvi and Evkeeza based on current regulations, our estimate of pricing on approval of Dojolvi and Evkeeza and other factors. However, if pricing is approved at levels lower than estimated, if at all, or if there are further changes in the regulatory framework, we may be required to pay back amounts higher than clawback reserves and reverse revenue that has been previously recorded.

Moreover, increasing efforts by governmental and third-party payors in the U.S. and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for new products and, as a result, they may not cover or provide adequate payment for our products and product candidates. We expect to experience pricing pressures in connection with the sale of any of our products and product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, additional legislative changes, including the impact from the Inflation Reduction Act of 2022, and statements by elected officials. For example, proposals have been discussed to tie U.S. drug prices to the cost in other countries, several states in the U.S. have introduced legislation to require pharmaceutical companies to disclose their costs to justify the prices of their products. Drug pricing is also expected to remain a focus for the current Presidential Administration and Congress. The downward pressure on healthcare costs in general, and with respect to prescription drugs, surgical procedures, and other treatments in particular, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain effective patent rights for our products, product candidates, or any future product candidates, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, trade secret protection, and confidentiality agreements to protect the intellectual property related to our technologies, our products, and our product candidates. Our success depends in large part on our and our licensors' ability to obtain and maintain patent and other intellectual property protection in the U.S. and in other countries with respect to our proprietary technologies, our products, and our product candidates.

We have sought to protect our proprietary position by filing patent applications in the U.S. and abroad related to our novel technologies, products and product candidates that are important to our business. This process is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain and involves complex legal and factual questions for which legal principles remain unsettled. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our products or product candidates in the U.S. or in foreign countries. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which can prevent a patent from issuing from a pending patent application or provide the basis for third parties to challenge the validity of an issued patent. Third parties may challenge the validity, enforceability, or scope of any issued patents, which may result in such patents being narrowed, found unenforceable, or invalidated. Furthermore, even if the patents and patent applications we own or in-license are unchallenged, they may not adequately protect our intellectual property, provide exclusivity for our products or product candidates, or prevent others from designing around our claims. Any of these outcomes could impair our ability to prevent competition from third parties.

We, independently or together with our licensors, have filed several patent applications covering various aspects of our products or product candidates. We cannot offer any assurances about which, if any, patent applications will issue, the breadth of any issued patent, or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful opposition to these patents could impair the exclusivity position of our products or deprive us of rights necessary for the successful commercialization of any product candidates that are approved. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

Our current patents or applications covering methods of use and certain compositions of matter do not provide complete patent protection for our products and product candidates in all territories. For example, there are no issued patents covering the Crysvita composition of matter in Latin America, where we have rights to commercialize this product. Therefore, a competitor could develop the same antibody or a similar antibody as well as other approaches that target FGF23 for potential commercialization in Latin America, subject to any intellectual property rights or regulatory exclusivities awarded to us. If we cannot obtain and maintain effective patent rights for our products or product candidates, we may not be able to compete effectively and our business and results of operations would be harmed.

We may not have sufficient patent terms to effectively protect our products and business.

Patents have a limited lifespan. In the U.S., the natural expiration of a patent is generally 20 years from its earliest non-provisional filing date. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if patents covering our products or product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic or biosimilar medications.

Patent term extensions under the Hatch-Waxman Act in the U.S. and under supplementary protection certificates in Europe may not be available to extend the patent exclusivity term for our products and product candidates, and we cannot provide any assurances that any such patent term extension will be obtained and, if so, for how long. Furthermore, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents, or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we do not have sufficient patent terms or regulatory exclusivity to protect our products, our business and results of operations may be adversely affected.

Patent law and rule changes could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

Changes in either the patent laws or interpretation of the patent laws in the U.S. and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the U.S. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. We therefore cannot be certain that we or our licensors were the first to make the inventions claimed in our owned and in-licensed patents or pending applications, or that we or our licensor were the first to file for patent protection of such inventions.

In 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law and introduced significant changes to the prosecution of U.S. patent applications and to the procedures for challenging U.S. patents. The effects of these changes remain unclear owing to the evolving nature of the law and the lengthy timelines associated with court system review and interpretation. Consequently, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

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

If we are unable to maintain effective proprietary rights for our products, product candidates, or any future product candidates, we may not be able to compete effectively in our markets.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our products or product candidate discovery and development processes that involve proprietary know-how, information, or technology that is not covered by patents. However, trade secrets can be difficult to protect. The confidentiality agreements entered into with our employees, consultants, scientific advisors, contractors and other third parties that we rely on in connection with the development, manufacture and commercialization of our products may not be sufficient to protect our proprietary technology and processes, which increase the risk that such trade secrets may become known by our competitors or may be inadvertently incorporated into the technology of others.

The physical security of our premises and physical and electronic security of our information technology systems may not preserve the integrity and confidentiality of our data and trade secrets. These individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

The assignment agreements we enter into with our employees and consultants to assign their inventions to us, and the confidentiality agreements we enter into with our employees, consultants, advisors, and any third parties who have access to our proprietary know-how, information, or technology may not have been duly executed and we cannot assure that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret.

Claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of others. There have been many lawsuits and other proceedings involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, inter partes reviews, post grant reviews, oppositions, and reexamination proceedings before the USPTO and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by other parties, exist in the fields in which we are developing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our products or product candidates may be subject to claims of infringement of the patent rights of these other parties.

Other parties may assert that we are employing their proprietary technology without authorization. There may be patents or patent applications with claims to materials, formulations, methods of manufacture, or methods for treatment relevant to the use or manufacture of our products or product candidates. We have conducted freedom to operate analyses with respect only to our products and certain of our product candidates, and therefore we do not know whether there are any patents of other parties that would impair our ability to commercialize all of our product candidates. We also cannot guarantee that any of our analyses are complete and thorough, nor can we be sure that we have identified each and every patent and pending application in the U.S. and abroad that covers technology relevant or necessary to the commercialization of our products or product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that are relevant to our products or product candidates.

We are aware of certain U.S. and foreign patents owned by third parties that a court might construe to be valid and relevant to one or more of our gene therapy product candidates, certain methods that may be used in their manufacture or delivery, or certain formulations comprising one or more of our gene therapy candidates. Regarding our anti-sclerostin antibody product candidate, setrusumab, we are aware of litigation involving patents owned by a third-party, OssiFi-Mab LLC, or OMab, relating to methods of using sclerostin antagonists in combination with antiresorptive drugs to increase bone growth, bone formation, and/or bone density. Specifically, in the U.S., OMab has asserted certain patents expiring in 2027 or 2028 against Amgen based on Amgen's commercialization of an anti-sclerostin antibody, Evenity®, for the treatment of osteoporosis in postmenopausal women at high risk for fracture; Amgen denies infringement and asserts the OMab patents are invalid. In Europe, OMab was granted two patents with related subject matter; the first patent has been revoked while the second has been opposed by Amgen, UCB, and two anonymous parties. There is a risk that one or more third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that one or more of these patents is valid, enforceable, and infringed, in which case the owners of any such patents may be able to block our ability to commercialize a product candidate unless we obtain a license under the applicable patents, or until such patents expire. However, such a license may not be available on commercially reasonable terms or at all.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to continue commercialization of our products, or block our ability to develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products, or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

Because our programs may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license, or use these proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes, or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources, and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We sometimes collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the corresponding program.

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

Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, we may face competition from biosimilars with respect to our biological products (Crysvita, Mepsevii and Evkeeza) and our biological product candidates. In the U.S., the Biologics Price Competition and Innovation Act of 2009, or BPCI Act, was included in the Affordable Care Act and created an abbreviated approval pathway for biological products that are demonstrated to be "highly similar," or biosimilar, to or "interchangeable" with an FDA-approved biological product. The BPCI Act prohibits the FDA from approving a biosimilar or interchangeable product that references a brand biological product until 12 years after the licensure of the reference product, but permits submission of an application for a biosimilar or interchangeable product to the FDA four years after the reference product was first licensed. The BPCI Act does not prevent another company from developing a product that is highly similar to the innovative product, generating its own data, and seeking approval. The law is complex and is still being interpreted and implemented by the FDA. Moreover, aspects of the law are still being evaluated and interpreted by courts. As a result, its ultimate impact, implementation and meaning are subject to uncertainty. Modification of the BPCI Act, or changes to the interpretation or implementation of the BPCI Act, could have a material adverse effect on the future commercial prospects for our biological products and product candidates.

In Europe, the European Commission has granted marketing authorizations for several biosimilars pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In Europe, a competitor may reference data supporting approval of an innovative biological product, but will not be able to get on the market until 10 years after the time of approval of the innovative product. This 10-year marketing exclusivity period will be extended to 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. In addition, companies may be developing biosimilars in other countries that could compete with our products.

If competitors are able to obtain marketing approval for biosimilars referencing our products, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences

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

Under the Hatch-Waxman Act, a pharmaceutical manufacturer may file an abbreviated new drug application, or ANDA, seeking approval of a generic copy of an approved, innovator small-molecule product such as Dojolvi. Under the Hatch-Waxman Act, a manufacturer may also submit an NDA under section 505(b)(2) that references the FDA's finding of safety and effectiveness of a previously approved innovator small-molecule product. A 505(b)(2) NDA product may be for a new or improved version of the original innovator product. Innovative small-molecule drugs may be eligible for certain periods of regulatory exclusivity (e.g., five years for new chemical entities, three years for changes to an approved drug requiring a new clinical study, and seven years for orphan drugs), which preclude FDA approval (or in some circumstances, FDA filing and review of) an ANDA or 505(b)(2) NDA relying on the FDA's finding of safety and effectiveness for the innovative drug. In addition to the benefits of regulatory exclusivity, an innovator NDA holder may have patents claiming the active ingredient, product formulation or an approved use of the drug, which would be listed with the product in the "Orange Book." If there are patents listed in the Orange Book, a generic applicant that seeks to market its product before expiration of the patents must include in the ANDA or 505(b)(2) what is known as a "Paragraph IV certification," challenging the validity or enforceability of, or claiming non-infringement of, the listed patent or patents. Notice of the certification must be given to the innovator, too, and if within 45 days of receiving notice the innovator sues to enforce its patents, approval of the ANDA is stayed for 30 months, or as lengthened or shortened by the court.

During the year ended December 31, 2024, Navinta, Aurobindo, and Esjay filed ANDAs for generic versions of Dojolvi. We have filed a patent infringement suit under the Hatch-Waxman Act against Navinta, Aurobindo and Esjay in the United States District Court for the District of New Jersey in response to the notices. See "Item 1. Legal Proceedings" above for a description of our suit. We cannot predict the outcome of our suit, nor can we predict whether there will be additional ANDA filings for Dojolvi.

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

We may not be successful in securing or maintaining proprietary patent protection for products and technologies we develop or license. Moreover, if any patents that are granted and listed in the Orange Book are successfully challenged by way of a Paragraph IV certification and subsequent litigation, the affected product could more immediately face generic competition and its sales would likely decline materially. For instance, if the existing ANDA filers or additional competitors are able to enter the market with generic versions of Dojolvi, our sales of Dojolvi could materially decline which could have an adverse impact on our financial results.

The patent protection and patent prosecution for some of our products and product candidates is dependent on third parties.

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

In addition, we have in-licensed various patents and patent applications owned by the University of Pennsylvania relating to our DTX301, DTX401 and/or UX701 product candidates. Some of these patents and patent applications are licensed or sublicensed by REGENX and sublicensed to us. We do not have the right to control the prosecution of these patent applications, or the maintenance of any of these patents. In addition, under our agreement with REGENX, we do not have the first right to enforce the licensed patents, and our enforcement rights are subject to certain limitations that may adversely impact our ability to use the licensed patents to exclude others from commercializing competitive products. Moreover, REGENX and the University of Pennsylvania may have interests which differ from ours in determining whether to enforce and the manner in which to enforce such patents.

If KKC, Regeneron, the University of Pennsylvania, REGENX, or any of our future licensing partners fail to appropriately prosecute, maintain, and enforce patent protection for the patents covering any of our products or product candidates, our ability to develop and commercialize those products or product candidates may be adversely affected and we may not be able to prevent competitors from making, using, and selling competing products. In addition, even where we now have the right to control patent prosecution of patents and patent applications we have licensed from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to us assuming control over patent prosecution.

If we fail to comply with our obligations in the agreements under which we license intellectual property and other rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are a party to a number of intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty, and other obligations on us. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, we may be required to make certain payments to the licensor, we may lose the exclusivity of our license, or the licensor may have the right to terminate the license, in which event we would not be able to develop or market products covered by the license. Additionally, the milestone and other payments associated with these licenses will make it less profitable for us to develop our product candidates.

In certain cases, we control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners. Licensing of intellectual property is of critical importance to our business and involves complex legal, business, and scientific issues. Disputes may arise regarding intellectual property subject to a licensing agreement, including but not limited to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;

- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our collaborators; and
- the priority of invention of patented technology.

If disputes over intellectual property and other rights that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

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

Competitors have in the past and may in the future infringe our patents or the patents of our licensors. If we or one of our licensing partners were to initiate legal proceedings against a third party to enforce a patent covering our products or one of our product candidates, the defendant could counterclaim that the patent covering our product or product candidate is invalid and/or unenforceable. For example, in September 2024, we filed a patent infringement suit under the Hatch-Waxman Act against Navinta, Aurobindo and Esjay. See " Item 1. Legal Proceedings" above for more information regarding our suit. In patent litigation in the U.S., defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable.

Interference proceedings or derivation proceedings now available under the Leahy-Smith Act provoked by third parties or brought by us or declared or instituted by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. In addition, the validity of our patents could be challenged in the USPTO by one of the new post grant proceedings (*i.e., inter partes* review or post grant review) now available under the Leahy-Smith Act. Our defense of litigation, interference proceedings, or post grant proceedings under the Leahy-Smith Act may fail and, even if successful, may result in substantial costs and distract our management and other employees.

We may in the future also be subject to claims that former employees, collaborators, or other third parties have an interest in our patents as an inventor or co-inventor. In addition, we may have ownership disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail to successfully defend against such litigation or claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property.

Even if we are successful in defending against such litigation and claims, such proceedings could result in substantial costs and distract our management and other employees. Because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments related to such litigation or claims. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

We employ certain individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Our efforts to vet our employees, consultants, and independent contractors and prevent their use of the proprietary information or know-how of others in their work for us may not be successful, and we may in the future be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distract management and other employees.

Changes to patent laws in the U.S. and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology and pharmaceutical industries involves both technological and legal complexity. Therefore, obtaining and enforcing such patents is costly, time consuming, and inherently uncertain.

In recent years, the U.S. Supreme Court has ruled on several patent cases, and in some instances, narrowed the scope of patent protection available. In addition, there have been recent proposals for changes to U.S. laws that, if adopted, could impact our ability to obtain or maintain patent protection for our proprietary technologies. Depending on future actions by U.S. courts, U.S. Congress, the USPTO, and the relevant lawmaking bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents, shorten the term of our existing patents and patents that we might obtain in the future, or impair the validity or enforceability of our patents that may be asserted against our competitors or other third parties. Any of these outcomes could have a material adverse effect on our business.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting, and defending patents on our products or product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U.S. can be less extensive than those in the U.S. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the U.S. Further, licensing partners such as KKC and Regeneron may not prosecute patents in certain jurisdictions in which we may obtain commercial rights, thereby precluding the possibility of later obtaining patent protection in these countries. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection, but enforcement is not as strong as that in the U.S. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Risks Related to Our Business Operations

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

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

specifications and other requirements. If we fail to comply with these requirements, we would be subject to possible regulatory action and may not be permitted to sell any products that we may develop.

As we seek to optimize and operate our manufacturing process at the facility, we will likely face technical and scientific challenges, considerable capital costs and potential difficulty in recruiting and hiring experienced, qualified personnel at the facility which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements. We may also experience unexpected technical, regulatory, safety, quality or operational issues during manufacturing campaigns. As we expand our commercial footprint to multiple geographies, we may establish multiple manufacturing facilities, which may lead to regulatory delays or prove costly. Even if we are successful, we cannot assure that such additional capacity will be required or that our investment will be recouped. Further, our manufacturing capabilities could be affected by cost-overruns, unexpected delays, equipment failures, lack of capacity, labor shortages, natural disasters, power failures, program failures, actual or threatened public health emergencies, and numerous other factors that could prevent us from realizing the intended benefits of our manufacturing strategy.

Our future success depends in part on our ability to retain our Founder, President, and Chief Executive Officer and to attract, retain, and motivate other qualified personnel.

We are dependent on Emil D. Kakkis, M.D., Ph.D., our Founder, President, and Chief Executive Officer, the loss of whose services may adversely impact the achievement of our objectives. Dr. Kakkis could leave our employment at any time, as he is an "at will" employee. Recruiting and retaining other qualified employees, consultants, and advisors for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled personnel in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. In addition, failure to succeed in preclinical or clinical studies may make it more challenging to recruit and retain qualified personnel. The inability to recruit and retain qualified personnel, or the loss of the services of Dr. Kakkis or any of other member of our executive leadership team or other key employee, may impede the progress of our research, development, and commercialization objectives.

If we fail to obtain or maintain orphan drug exclusivity for our products, our competitors may sell products to treat the same conditions and our revenue will be reduced. If another party obtains orphan drug exclusivity for a product that is essentially the same as a product we are developing for a particular indication, we may be precluded or delayed from commercializing the product in that indication.

Our business strategy focuses on the development of drugs that are eligible for FDA and EU orphan drug designation. In the U.S., orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical study costs, tax advantages, and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity. In the EU, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following drug or biological product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Because the extent and scope of patent protection for our products may in some cases be limited, orphan drug designation is especially important for our products for which orphan drug designation may be available. For eligible drugs, we plan to rely on the exclusivity period under the Orphan Drug Act to maintain a competitive position. If we do not obtain orphan drug exclusivity for our drug products and biologic products that do not have broad patent protection, our competitors may then sell the same drug to treat the same condition sooner than if we had obtained orphan drug exclusivity, and our revenue will be reduced. Additionally, if a competitor obtains approval of the same drug for the same indication before us, and the FDA grants such orphan drug exclusivity, we would be prohibited from obtaining approval for our product for seven or more years, unless our product can be shown to be clinically superior.

Even though we have orphan drug designation for UX111, UX143, DTX301, DTX401 and UX701 in the U.S. and Europe and for GTX 102 in the U.S., we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition or the same drug can be approved for a different indication unless there are other exclusivities such as new chemical entity exclusivity preventing such approval. Even after an orphan drug is approved, the FDA or EMA can subsequently approve the same drug with the same active moiety for the same condition if the FDA or EMA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

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

We have recorded on our 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 Condensed Consolidated Statement of Operations. We have not recorded any impairments related to our intangible assets through March 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. Research programs to identify and develop new product candidates require substantial technical, financial, and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. Our research programs or licensing efforts may fail to yield additional product candidates for clinical development and commercialization for a number of reasons, including but not limited to the following:

- our research or business development methodology or search criteria and process may be unsuccessful in identifying potential product candidates;
- we may not be able or willing to assemble sufficient technical, financial or human resources to acquire or discover additional product candidates;
- we may face competition in obtaining and/or developing additional product candidates;
- our product candidates may not succeed in research, discovery, preclinical or clinical testing;
- our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop may be covered by third parties' patents or other exclusive rights;
- the market for a product candidate may change during our program so that such a product may become unreasonable to continue to develop;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost or at all; and
- a product candidate may not be accepted as safe and effective by regulatory authorities, patients, the medical community, or payors.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, or we may not be able to identify, license, discover, develop, or commercialize additional product candidates, which would have a material adverse effect on our business and could potentially cause us to cease operations.

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

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

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

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

As described under "Item 1. Business – Government Regulation" of our Annual Report and in the Risk Factor above entitled *" – The insurance coverage and reimbursement status of newly approved products is uncertain"* there have been and continue to be a number of legislative initiatives to contain healthcare costs and to modify the regulation of drug and biologic products. We expect that additional state and federal healthcare reform measures and regulations will be adopted in the future, including proposals to reduce the exclusivity protections provided to already approved biological products and to provide biosimilar and interchangeable biologic products an easier path to approval. Any of these measures and regulations could limit the amounts that federal and state governments will pay for healthcare products and services, result in reduced demand for our product candidates or additional pricing pressures and affect our product development, testing, marketing approvals and post-market activities.

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

Our business is subject to evolving regulation by various federal, state, local and foreign governmental agencies, including agencies responsible for monitoring and enforcing employment and labor laws, workplace safety, privacy and security laws and regulations, and tax laws and regulations. In certain jurisdictions, these regulatory requirements may be more stringent than those in the U.S., and in other circumstances these requirements may less stringent than those in the U.S.

In particular, our operations are directly, and indirectly through our customers, subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and physician sunshine laws and regulations; and patient and non-patient privacy regulations, including the GDPR and the California Consumer Privacy Act, or CCPA, including amendments from the California Privacy Rights Act, or CPRA, as described in "Item 1. Business – Government Regulation" of our Annual Report. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. For instance, one of our programs for sponsored genetic testing to help patients receive an accurate diagnosis was previously the subject of review by applicable governmental authorities of compliance with various fraud and abuse laws. We settled the matter with the governmental authorities for an immaterial settlement amount and without any admission of legal liability. We cannot assure that our other operations or programs will not be subject to review by governmental authorities or found to violate such laws.

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

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, disgorgement of profits, and the curtailment or restructuring of our operations. If any governmental sanctions, fines, or penalties are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, operating results, financial condition and our reputation could be harmed. In addition, responding to any action will likely result in a significant diversion of management's attention and resources and an increase in professional fees.

Our research and development activities, including our process and analytical development activities in our quality control laboratory, and our and our third-party manufacturers' and suppliers' activities, including activities related to the build-out and operation of our gene therapy manufacturing facility, involve the controlled storage, use, and disposal of hazardous materials, including the components of our product candidates, such as viruses, and other hazardous compounds, which subjects us to laws and regulations governing such activities. In some cases, these hazardous materials and various wastes resulting from their use are stored at our or our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts, and business operations or environmental damage that could result in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. We cannot guarantee that the safety procedures utilized by us and our third-party manufacturers for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages—and such liability could exceed our resources—and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently, and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance.

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

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

Our business strategy includes international expansion. We currently conduct clinical studies and regulatory activities and we also commercialize products outside of the U.S. An increasing portion of our revenues are based on our international operations, which exposes us to increased financial risks such as longer payment cycles, additional or more burdensome regulatory requirements of financial institutions outside of the U.S. and exposure to foreign currency exchange rate. We may implement currency hedges intended to reduce our exposure to changes in certain foreign currency exchange rates. However, our hedging strategies, if implemented, may not be successful, and any of our unhedged foreign exchange exposures will continue to be subject to market fluctuations. Further, we sell products in countries that face economic volatility and weakness. Although we have historically collected receivables from customers in those countries, continued weakness or additional deterioration of the local economies and currencies may cause customers in those countries to be unable to pay for our products. Additionally, if one or more of these countries were unable to purchase our products, our revenues would be adversely affected. 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. Although these tariffs do not currently include pharmaceutical products, the current Presidential Administration has threatened imposing such tariffs and there can be no assurance that future tariffs or other governmental trade actions will not impact pharmaceutical products or the active ingredients or materials used in such products, 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.

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

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

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

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

Our business and operations may be materially adversely affected in the event of computer system failures or security breaches.

Cybersecurity incidents, including phishing attacks and attempts to misappropriate or compromise confidential or proprietary information or sabotage enterprise IT systems are becoming increasingly frequent and more sophisticated. Cybersecurity incidents increasingly involve the use of AI and machine learning to launch more automated, targeted and coordinated attacks on targets. The information and data processed and stored in our technology systems, and those of our strategic partners, CROs, contract manufacturers, suppliers, distributors or other third parties for which we depend to operate our business, may be vulnerable to loss, damage, denial-of-service, unauthorized access or misappropriation. Data security breaches can occur as a result of malware, hacking, business email compromise, ransomware attacks, phishing or other cyberattacks directed by third parties. We, and certain of the third parties for which we depend on to operate our business, have experienced cybersecurity incidents, including third party unauthorized access to and misappropriation of financial information and clinical data, and may experience similar incidents in the future. Further, risks of unauthorized access and cyber-attacks have increased as most of our personnel, and the personnel of many third parties with which we do business, have adopted hybrid working arrangements. Improper or inadvertent behavior by employees, contractors and others with permitted access to our systems, including through the use of generative AI technologies, pose a risk that sensitive data may be exposed to unauthorized persons or to the public. A system failure or security breach that interrupts our operations or the operations at one of our third-party vendors or partners could result in intellectual property and other proprietary or confidential information being lost or stolen or a material disruption of our drug development programs and commercial operations. For example, the loss of clinical trial data from ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, loss of trade secrets or inappropriate disclosure of confidential or proprietary information, including protected health information, or personal information of employees or former employees, access to our clinical data, or disruption of the manufacturing process, we could incur liability and the further development of our drug candidates could be delayed. Further, we could incur significant costs to investigate and mitigate such cybersecurity incidents. In addition, there can be no assurance that our insurance coverage will be sufficient to cover the financial, legal, business or reputational losses that may result from a cybersecurity incident. A security breach that results in the unauthorized access, use or disclosure of personal information also requires us to notify individuals, governmental authorities, credit reporting agencies, or other parties, as applicable, pursuant to privacy and security laws and regulations or other obligations. Such a security breach could harm our reputation, erode confidence in our information security measures, and lead to regulatory scrutiny and result in penalties, fines, indemnification claims, litigation and potential civil or criminal liability.

We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our corporate headquarters and one of our laboratories are located in the San Francisco Bay Area, and our collaboration partner for Crysvita, KKC, is located in Japan, which have both in the past experienced severe earthquakes and other natural disasters. We do not carry earthquake insurance. Earthquakes or other natural disasters could severely disrupt our operations or those of our collaborators, and have a material adverse effect on our business, results of operations, financial condition, and prospects. We have also experienced power outages as a result of wildfires in the San Francisco Bay Area which are likely to continue to occur in the future. If a natural disaster, power outage, or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure (such as the manufacturing facilities of our third-party contract manufacturers) or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and may be inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

We may acquire companies or products or engage in strategic transactions, which could divert our management's attention and cause us to incur various costs and expenses, or result in fluctuations with respect to the value of such investment, which could impact our operating results.

We may acquire or invest in businesses or products that we believe could complement or expand our business or otherwise offer growth opportunities. For example, we acquired Dimension in November 2017 and GeneTx in July 2022. The pursuit of potential acquisitions or investments may divert the attention of management and may cause us to incur various costs and expenses in identifying, investigating, and pursuing them, whether or not they are consummated. We may not be able to identify desirable acquisitions or investments or be successful in completing or realizing anticipated benefits from such transactions. We may experience difficulties in assimilating the personnel, operations and products of the acquired companies, management's attention may be diverted from other business concerns and we may potentially lose key employees of the acquired company. If we are unable to successfully or timely integrate the operations of acquired companies with our business, we may incur unanticipated liabilities and be unable to realize the revenue growth, synergies and other anticipated benefits resulting from the acquisition, and our business, results of operations and financial condition could be materially and adversely affected.

The value of our investments in other companies or businesses may also fluctuate significantly and impact our operating results quarter to quarter or year to year. We purchased 7,825,797 shares of common stock of Solid in October 2020. Our investment in Solid is being accounted for at fair value, as the fair value is readily determinable. As a result, increases or decreases in the stock price of equity investments have resulted in and will result in accompanying changes in the fair value of our investments, and cause substantial volatility in, our operating results for the reporting period. As the fair value of our investment in Solid is dependent on the stock price of Solid, which has recently seen wide fluctuations, the value of our investments and the impact on our operating results may similarly fluctuate significantly from quarter to quarter and year to year such that period-to-period comparisons may not be a good indication of the future value of the investments and our future operating results.

Risks Related to Ownership of Our Common Stock

The market price of our common stock may be highly volatile.

The market price of our common stock has been, and is likely to continue to be, volatile, including for reasons unrelated to changes in our business. Our stock price could be subject to wide fluctuations in response to a variety of factors, including but not limited to the following:

- adverse results or delays in preclinical or clinical studies;
- any inability to obtain additional funding;
- any delay in filing an IND, NDA, BLA, MAA, or other regulatory submission for any of our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory agency's review of that IND, NDA, BLA, MAA, or other regulatory submission;
- the perception of limited market sizes or pricing for our products and product candidates;
- decisions by our collaboration partners with respect to the indications for our products and product candidates in countries where they have the right to commercialize the products and product candidates;
- decisions by our collaboration partners regarding market access and pricing in countries where they have the right to commercialize our products and product candidates;

- failure to successfully develop and commercialize our products and product candidates;
- the level of revenue we receive from our commercialized products or from named patient sales;
- post-marketing safety issues;
- failure to maintain our existing strategic collaborations or enter into new collaborations;
- failure by us or our licensors and strategic collaboration partners to prosecute, maintain, or enforce our intellectual property rights;
- changes in laws or regulations applicable to our products;
- any inability to obtain adequate product supply for our products and product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products, services, or technologies by our competitors;
- changes in or failure to meet or exceed financial projections or other guidance we may provide to the public;
- changes in or failure to meet or exceed the financial projections or other expectations of the investment community;
- the perception of the pharmaceutical industry or our company by the public, legislatures, regulators, and the investment community;
- the perception of the pharmaceutical industry's approach to drug pricing;
- announcements of significant acquisitions, strategic partnerships, joint ventures, or capital commitments by us, our strategic collaboration partners, or our competitors;
- the integration and performance of any businesses we have acquired or may acquire;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant investigations, regulatory proceedings or lawsuits, including patent or stockholder litigation;
- securities or industry analysts' reports regarding our stock, or their failure to issue such reports;
- changes in the market valuations of similar companies;
- general market, macroeconomic conditions or geopolitical developments, changing interest rates, 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 March 31, 2025, there were 3,235,021 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 March 31, 2025, there were 6,409,256 shares available for issuance under the A&R ESPP.

Our board of directors has adopted an Employment Inducement Plan, which was amended in July 2024, or the Inducement Plan, with a maximum of 1,200,000 shares available for grant under the plan. At March 31, 2025, there were 205,258 shares available for issuance under the Inducement Plan. If our board of directors elects to increase the number of shares available for future grant under the 2023 Plan, the A&R ESPP, or the Inducement Plan, our stockholders may experience additional dilution, which could cause our stock price to fall.

Provisions in our amended and restated certificate of incorporation and by-laws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders, or remove our current management.

Our amended and restated certificate of incorporation, amended and restated by-laws, and Delaware law contain provisions that may have the effect of delaying or preventing a change in control of us or changes in our management. Our amended and restated certificate of incorporation and by-laws include provisions that:

- authorize “blank check” preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend, and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors or the chairperson of our board of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed only for cause;
- provide that vacancies on our board of directors may be filled only by a resolution adopted by the board of directors;
- expressly authorize our board of directors to modify, alter or repeal our amended and restated bylaws; and
- require holders of 75% of our outstanding common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated by-laws.

These provisions, alone or together, could delay, deter, or prevent hostile takeovers and changes in control or changes in our management.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Further, no stockholder is permitted to cumulate votes at any election of directors because this right is not included in our amended and restated certificate of incorporation.

Any provision of our amended and restated certificate of incorporation or amended and restated by-laws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

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

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

General Risk Factors

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

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. In particular, we are required to perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting, as required by Section 404(a) of the Sarbanes-Oxley Act. Section 404(b) of the Sarbanes-Oxley Act also requires our independent auditors to attest to, and report on, this management assessment. Ensuring that we have adequate internal controls in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that will need to be evaluated frequently. If we are not able to comply with the requirements of Section 404 or if we or our independent registered public accounting firm are unable to attest to the effectiveness of our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC, or other regulatory authorities, which would require additional financial and management resources.

We may incur additional tax liabilities related to our operations.

We have a multinational tax structure and are subject to income tax in the U.S. and various foreign jurisdictions. Our effective tax rate is influenced by many factors including changes in our operating structure, changes in the mix of our earnings among countries, our allocation of profits and losses among our subsidiaries, our intercompany transfer pricing agreements and rules relating to transfer pricing, the availability of U.S. research and development tax credits, and future changes in tax laws and regulations in the U.S. and foreign countries. Significant judgment is required in determining our tax liabilities including management's judgment for uncertain tax positions. The Internal Revenue Service, other domestic taxing authorities, or foreign taxing authorities may disagree with our interpretation of tax laws as applied to our operations. Our reported effective tax rate and after-tax cash flows may be materially and adversely affected by tax assessments in excess of amounts accrued for our financial statements. This could materially increase our future effective tax rate thereby reducing net income and adversely impacting our results of operations for future periods.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history. To the extent that we continue to generate taxable losses, unused taxable losses will, subject to certain limitations, carry forward to offset future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the IRC, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOL carryforwards, and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. An analysis to determine limitations upon our NOL carryforwards and other pre-change tax attributes for ownership changes that have occurred previously has been performed, resulting in a permanent decrease of federal and state NOL carryforwards in the amount of $7.2 million and a permanent decrease in federal research tax credit carryforwards in the amount of $0.2 million. As a result of these decreases and others that may occur as a result of future ownership changes, our ability to use our pre-change NOL carryforwards and other tax attribute carryforwards to offset U.S. federal taxable income and tax liabilities is limited and may become subject to even greater limitations, which could potentially accelerate or permanently increase future federal tax liabilities for us. In addition, there may be periods during which the use of state income tax NOL carryforwards and other state tax attribute carryforwards (such as state research tax credits) are suspended or otherwise limited, which could potentially accelerate or permanently increase future state tax liabilities for us.

Litigation may substantially increase our costs and harm our business.

We have been, and may in the future become, party to lawsuits including, without limitation, actions, claims and proceedings in the ordinary course of business relating to our directors, officers, stockholders, intellectual property, and employment matters and policies, which will cause us to incur legal fees and other costs related thereto, including potential expenses for the reimbursement of legal fees of officers and directors under indemnification obligations. For example, we have been defending a lawsuit filed in the U.S. District Court for the District of Maryland by the Estate of Henrietta Lacks alleging unjust enrichment arising from our receipt and use of HeLa cells. See also "Item 1. Legal Proceedings" above. The expense of defending against such claims or litigation may be significant and there can be no assurance that we will be successful in any defense. Further, the amount of time that may be required to resolve such claims or lawsuits is unpredictable, and these actions may divert management's attention from the day-to-day operations of our business, which could adversely affect our business, results of operations, and cash flows. Litigation is subject to inherent uncertainties, and an adverse result in such matters that may arise from time to time could have a material adverse effect on our business, results of operations, and financial condition.

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

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

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

Companies across all industries are facing increasing scrutiny relating to their Environmental, Social and Governance, or ESG, practices and disclosures and institutional and individual investors are increasingly using ESG screening criteria in making investment decisions. Investors 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 practices to satisfy all investors and stakeholders, and our reputation, our ability to attract or retain employees or our attractiveness as an investment could be negatively impacted. Further, investors who are focused on ESG matters may seek enhanced ESG disclosures or to implement policies adverse to our business, and there can be no assurances that stockholders will not advocate, via proxy contests, media campaigns or other public or private means, for us to make corporate governance changes or engage in certain corporate actions. Our disclosures on these matters or a failure to satisfy evolving stakeholder expectations for ESG practices and reporting may potentially harm our reputation and impact employee retention and access to capital. In addition, our failure, or perceived failure, to pursue or fulfill our goals, targets, and objectives or to satisfy various reporting standards within the timelines we announce, or at all, could expose us to government enforcement actions and private litigation.

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

Item 2. ***Unregistered Sales of Equity Securities and Use of Proceeds***

None.

Item 3. ***Defaults Upon Senior Securities***

None.

Item 4. ***Mine Safety Disclosures***

Not applicable.

Item 5. ***Other Information***

During the three months ended March 31, 2025 the following directors and Section 16 officers adopted a Rule 10b5-1 trading arrangement intended to satisfy the affirmative defense conditions of Rule 10b5-1(c).

Name and Title	Date Adopted	Aggregate Number of Shares of Common Stock to be Sold (Subject to Certain Conditions)	Plan End Date
Karah Parschauer, EVP, Chief Legal Officer and Corporate Affairs	March 11, 2025	Up to 54,601 shares	March 3, 2026
Emil D. Kakkis, M.D., Ph.D. President and CEO, Director	March 14, 2025	Up to 100,000 shares	March 17, 2026

Item 6. ***Exhibits***

		Incorporated by Reference			
Exhibit Number	**Exhibit Description**	**Form**	**Date**	**Number**	**Furnished or Filed Herewith**
3.1	Amended and Restated Certificate of Incorporation	8-K	2/5/2014	3.1	
3.2	Second Amended and Restated Bylaws	8-K	12/23/2023	3.1	
4.1	Form of Common Stock Certificate	S-1	11/8/2013	4.2	
4.2	Form of Indenture	S-3ASR	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	
10.1#	Form of Performance Stock Unit Agreement (2025)				X
31.1	Certification of Principal Executive Officer Required Under Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act				X
31.2	Certification of Principal Financial Officer Required Under Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act				X
32.1*	Certification of Principal Executive Officer and Principal Financial Officer Required Under Rule 13a-14(b) or Rule 15d-14(b) of the Exchange Act and 18 U.S.C. 1350				X
101.INS	XBRL Instance Document, formatted in Inline XBRL				X
101.SCH	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents				X
104	Cover Page Interactive Data File, formatted in Inline XBRL (included in Exhibit 101).				

# Indicates management contract or compensatory plan

* The certification attached as Exhibit 32.1 that accompanies this Quarterly Report is furnished to, and not deemed filed with, the SEC and is not to be incorporated by reference into any filing of the Registrant under the Securities Act or the Exchange Act, whether made before or after the date of this Form 10-Q, irrespective of any general incorporation language contained in such filing.

SIGNATURES

Pursuant to the requirements 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.

Date: May 6, 2025

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

Date: May 6, 2025

By: /s/ Howard Horn
Howard Horn
Executive Vice President, Chief Financial Officer, Corporate Strategy
(Principal Financial Officer)

Date: May 6, 2025

By: /s/ Theodore A. Huizenga
Theodore A. Huizenga
Senior Vice President and Chief Accounting Officer
(Principal Accounting Officer)

Exhibit 10.1

[***] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED BECAUSE THE INFORMATION (I) IS NOT MATERIAL AND (II) THE TYPE THAT THE REGISTRANT TREATS A PRIVATE OR CONFIDENTIAL.

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

ULTRAGENYX PHARMACEUTICAL INC.
2023 INCENTIVE PLAN

PERFORMANCE STOCK UNIT AGREEMENT (2025)

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

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

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

3. Vesting.

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

(b) The Revenue PSUs shall vest as follows:

(i) If the Administrator certifies that the revenue performance metric set forth in Appendix A attached hereto (the "Revenue Vesting Metric") has been achieved at at least the threshold level of performance during the period beginning on January 1, 2025 and ending on December 31, 2026 (the "Revenue Performance Period"), 100% of the Earned Revenue PSUs (as determined pursuant to Appendix A) shall vest on the later of (x) the date on which the Administrator certified such achievement and (y) March 1, 2027.

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

(c) If the Administrator certifies that the relative total stockholder return performance metric set forth in Appendix B attached hereto (the "TSR Vesting Metric") has been achieved at at least the threshold level of performance during the period beginning on January 1, 2025 and ending on December 31, 2027 (the "TSR and Strategic Performance Period"), 100% of the Earned TSR PSUs (as determined pursuant to Appendix B) shall vest on the later of (x) the date on which the Administrator certified such achievement and (y) March 1, 2028.

(d) If the Administrator certifies that the strategic performance metric set forth in Appendix C attached hereto (the "Strategic Vesting Metric") has been achieved by at least the threshold level of performance during the TSR and Strategic Performance Period, 100% of the Earned Revenue PSUs (as determined pursuant to Appendix C) shall vest on the later of (x) the date on which the Administrator certified such achievement and (y) March 1, 2028.

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

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

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

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

6. Forfeiture; Recovery of Compensation.

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

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

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

8. Certain Tax Matters.

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

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

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

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

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

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

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

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

ULTRAGENYX PHARMACEUTICAL INC.

By:
Name:
Title:

Dated:

Acknowledged and Agreed:

By:
[Grantee's Name]

APPENDIX A

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

	If UX143 Interim Analysis II Not Achieved:	If UX143 Interim Analysis II Achieved:	
Level of Performance	Aggregate GAAP Revenue[(1)] for FY 2025 and FY 2026	Aggregate GAAP Revenue[(1)] for FY 2025 and FY 2026	Earned Revenue PSUs[(2)]
Threshold	$[***]	$[***]	50%
Target	$[***]	$[***]	100%
Maximum	$[***]	$[***]	200%

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

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

APPENDIX B

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

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

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

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

(3) Notwithstanding the level of performance achieved pursuant to the foregoing table, in the event the Company's Total Stockholder Return is less than 0%, the percentage of the TSR PSUs that become Earned TSR PSUs will be no more than 100%.

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

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

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

APPENDIX C

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

Strategic Goals

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

Level of Performance	Number of Strategic Goals Achieved	Earned Revenue PSUs
Threshold	Achieve 1of Goals #1-#3 above	50%
Target	Achieve 2 of Goals #1-#3 above	100%
Stretch	Achieve 3 of Goals #1-#4 above	150%
Maximum	Achieve 4 of Goals #1-#4 above	200%

Exhibit 31.1

CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Emil D. Kakkis, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Ultragenyx Pharmaceutical Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of registrant's Board of Directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: May 6, 2025

/s/ Emil D Kakkis
Emil D. Kakkis, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Howard Horn, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Ultragenyx Pharmaceutical Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of registrant's Board of Directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: May 6, 2025

/s/ Howard Horn
Howard Horn
Executive Vice President, Chief Financial Officer, Corporate Strategy
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO SECTION 906 OF
THE SARBANES-OXLEY ACT OF 2002 (18 U.S.C. SECTION 1350)

In connection with the accompanying Quarterly Report of Ultragenyx Pharmaceutical Inc. (the "Company") on Form 10-Q for the quarter ended March 31, 2025 (the "Report"), I, Emil D. Kakkis, M.D., Ph.D., as President and Chief Executive Officer of the Company, and Howard Horn, as Executive Vice President and Chief Financial Officer, Corporate Strategy of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: May 6, 2025

/s/ Emil D. Kakkis
Emil D. Kakkis, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Dated: May 6, 2025

/s/ Howard Horn
Howard Horn
Executive Vice President, Chief Financial Officer, Corporate Strategy
(Principal Financial Officer)