REFINITIV

# DELTA REPORT

## 10-Q

RARE - ULTRAGENYX PHARMACEUTICAL

10-Q - JUNE 30, 2024 COMPARED TO 10-Q - MARCH 31, 2024

The following comparison report has been automatically generated

| TOTAL DELTAS | 717 |
|---|---|
| CHANGES | 185 |
| DELETIONS | 213 |
| ADDITIONS | 319 |





REFINITIV

**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, June 30, 2024**

**OR**

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

**For the transition period from to .**

**Commission File No. 001-36276**

# ULTRAGENYX PHARMACEUTICAL INC.

**(Exact name of registrant as specified in its charter)**

| **Delaware** | **27-2546083** |
|---|---|
| (State or other jurisdiction of incorporation or organization) | (I.R.S. Employer Identification No.) |
| **60 Leveroni Court**<br>**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 April 26, 2024 July 29, 2024, the registrant had 83,133,341 92,165,190 shares of common stock issued and outstanding.

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**ULTRAGENYX PHARMACEUTICAL INC.**

**FORM 10-Q FOR THE QUARTER ENDED March 31, 2024 JUNE 30, 2024**

**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 “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “forecast,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would,” or the negative of these words, or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our commercialization, marketing, and manufacturing capabilities and strategy;
- our expectations regarding the timing of clinical study commencements and reporting results from same;
- the timing and likelihood of regulatory approvals for our product candidates;
- the anticipated indications for our product candidates, if approved;
- the potential market opportunities for commercializing our products and product candidates;
- our expectations regarding the potential market size and the size of the patient populations for our products and product candidates, if approved for commercial use;
- estimates of our expenses, revenue, capital requirements, and our needs for additional financing;
- our ability to develop, acquire, and advance product candidates into, and successfully complete, clinical studies;
- the implementation of our business model and strategic plans for our business, products and product candidates and the integration and performance of any businesses have acquired or may acquire;
- the initiation, timing, progress, and results of ongoing and future preclinical and clinical studies, and our research and development programs;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our products and product candidates;
- our ability to maintain and establish collaborations or strategic relationships or obtain additional funding;
- our ability to maintain and establish relationships with third parties, such as contract research organizations, contract manufacturing organizations, suppliers, and distributors;
- our financial performance and the expansion of our organization;
- our ability to obtain supply of our products and product candidates;
- the scalability and commercial viability of our manufacturing methods and processes;
- developments and projections relating to our competitors and our industry;
- stagnating or worsening business and economic conditions and increasing geopolitical instability, including inflationary pressures, general economic slowdown or a recession, high interest rates, foreign exchange rate volatility, financial institution instability, and changes in monetary policy;
- the impact of market conditions and volatility on unrealized gains or losses on our nonqualified deferred compensation plan investments and our financial results; and
- other risks and uncertainties, including those listed under Part 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, 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, 2024 | December 31, 2023 | June 30, 2024 | December 31, 2023 |
|---|---|---|---|---|
| **ASSETS** | **ASSETS** | | **ASSETS** | |
| Current assets: | | | | |
| Cash and cash equivalents | $ 112,250 | $ 213,584 | $ 480,693 | $ 213,584 |
| Marketable debt securities | 299,830 | 363,625 | 283,128 | 363,625 |
| Accounts receivable, net | 100,253 | 73,390 | 105,982 | 73,390 |
| Inventory | 35,907 | 33,969 | 40,137 | 33,969 |
| Other assets | 47,727 | 47,616 | 54,700 | 47,616 |
| Total current assets | 595,967 | 732,184 | 964,640 | 732,184 |
| Property, plant, and equipment, net | 285,111 | 290,566 | 278,707 | 290,566 |
| Marketable debt securities | 156,581 | 199,901 | 110,669 | 199,901 |
| Intangible assets, net | 165,045 | 166,271 | 166,243 | 166,271 |
| Goodwill | 44,406 | 44,406 | 44,406 | 44,406 |
| Other assets | 59,970 | 57,685 | 53,772 | 57,685 |
| Total assets | $ 1,307,080 | $ 1,491,013 | $ 1,618,437 | $ 1,491,013 |
| **LIABILITIES AND STOCKHOLDERS' EQUITY** | **LIABILITIES AND STOCKHOLDERS' EQUITY** | | **LIABILITIES AND STOCKHOLDERS' EQUITY** | |
| Current liabilities: | | | | |
| Accounts payable | $ 40,972 | $ 42,114 | $ 59,807 | $ 42,114 |
| Accrued liabilities | 149,133 | 196,486 | 154,421 | 196,486 |
| Lease liabilities | 12,781 | 12,595 | 11,717 | 12,595 |
| Liabilities for sales of future royalties | 42,689 | 29,242 | 46,921 | 29,242 |
| Total current liabilities | 245,575 | 280,437 | 272,866 | 280,437 |
| Lease liabilities | 27,979 | 30,574 | 25,741 | 30,574 |
| Deferred tax liabilities | 30,058 | 30,058 | 30,058 | 30,058 |
| Liabilities for sales of future royalties | 848,725 | 862,325 | 842,157 | 862,325 |
| Other liabilities | 14,479 | 12,205 | 15,197 | 12,205 |
| Total liabilities | 1,166,816 | 1,215,599 | 1,186,019 | 1,215,599 |
| Stockholders' equity: | | | | |
| Preferred stock, par value of $0.001 per share—25,000,000 shares authorized; nil outstanding in 2024 and in 2023 | — | — | — | — |

| | | | | |
|---|---|---|---|---|
| Common stock, par value of $0.001 per share—250,000,000 shares authorized; outstanding—83,094,037 in 2024 and 82,315,590 in 2023 | 83 | 82 | | |
| Treasury stock, at cost, 63,575 in 2024 and 9,559 in 2023 | (3,332) | (432) | | |
| Common stock, par value of $0.001 per share—250,000,000 shares authorized; outstanding—92,135,384 in 2024 and 82,315,590 in 2023 | 92 | 82 | | |
| Treasury stock, at cost, 65,063 in 2024 and 9,559 in 2023 | (3,395) | (432) | | |
| Deferred compensation obligation | 3,332 | 432 | 3,395 | 432 |
| Additional paid-in capital | 3,698,957 | 3,662,346 | 4,123,364 | 3,662,346 |
| Accumulated other comprehensive income (loss) | (431) | 647 | (1,095) | 647 |
| Accumulated deficit | (3,558,345) | (3,387,661) | (3,689,943) | (3,387,661) |
| Total stockholders' equity | 140,264 | 275,414 | 432,418 | 275,414 |
| Total liabilities and stockholders' equity | $ 1,307,080 | $ 1,491,013 | $ 1,618,437 | $ 1,491,013 |

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, | | Three Months Ended June 30, | | Six Months Ended June 30, | |
|---|---|---|---|---|---|---|
| | 2024 | 2023 | 2024 | 2023 | 2024 | 2023 |
| Revenues: | | | | | | |
| Product sales | $ 62,489 | $ 44,229 | $ 73,805 | $ 42,179 | $ 136,294 | $ 86,408 |
| Royalty revenue | 46,344 | 4,882 | 73,221 | 46,331 | 119,565 | 51,213 |
| Collaboration and license | — | 51,385 | — | 19,799 | — | 71,184 |
| Total revenues | 108,833 | 100,496 | 147,026 | 108,309 | 255,859 | 208,805 |
| Operating expenses: | | | | | | |
| Cost of sales | 17,533 | 12,257 | 21,280 | 9,914 | 38,813 | 22,171 |
| Research and development | 178,487 | 165,698 | 161,503 | 164,949 | 339,990 | 330,647 |
| Selling, general and administrative | 78,160 | 76,646 | 80,604 | 81,403 | 158,764 | 158,049 |
| Total operating expenses | 274,180 | 254,601 | 263,387 | 256,266 | 537,567 | 510,867 |
| Loss from operations | (165,347) | (154,105) | (116,361) | (147,957) | (281,708) | (302,062) |
| Interest income | 8,824 | 6,290 | 7,401 | 5,964 | 16,225 | 12,254 |
| Change in fair value of equity investments | 3,746 | (334) | (3,991) | 261 | (245) | (73) |
| Non-cash interest expense on liabilities for sales of future royalties | (15,847) | (15,636) | (15,960) | (15,375) | (31,807) | (31,011) |
| Other income (expense) | (1,605) | 308 | | | | |
| Other expense | (1,829) | (1,989) | (3,434) | (1,681) | | |
| Loss before income taxes | (170,229) | (163,477) | (130,740) | (159,096) | (300,969) | (322,573) |
| Provision for income taxes | (455) | (495) | (858) | (732) | (1,313) | (1,227) |
| Net loss | $ (170,684) | $ (163,972) | $ (131,598) | $ (159,828) | $ (302,282) | $ (323,800) |
| Net loss per share, basic and diluted | $ (2.03) | $ (2.33) | $ (1.52) | $ (2.25) | $ (3.54) | $ (4.58) |
| Shares used in computing net loss per share, basic and diluted | 84,286,292 | 70,368,478 | 86,580,516 | 70,897,991 | 85,433,443 | 70,639,015 |

See accompanying notes.

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

| | Three Months Ended March 31, | | Three Months Ended June 30, | | Six Months Ended June 30, | |
|---|---|---|---|---|---|---|
| | 2024 | 2023 | 2024 | 2023 | 2024 | 2023 |
| Net loss | $ (170,684) | $ (163,972) | $ (131,598) | $ (159,828) | $ (302,282) | $ (323,800) |
| Other comprehensive income (loss): | | | | | | |
| Foreign currency translation adjustments | 129 | 144 | (219) | 293 | (90) | 437 |
| Unrealized gain (loss) on available-for-sale securities | (1,207) | 2,462 | (445) | 576 | (1,652) | 3,038 |
| Other comprehensive income (loss): | (1,078) | 2,606 | (664) | 869 | (1,742) | 3,475 |
| Total comprehensive loss | $ (171,762) | $ (161,366) | $ (132,262) | $ (158,959) | $ (304,024) | $ (320,325) |

See accompanying notes.



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

| | Common Stock | | Additional Paid-In Capital | Accumulated Other Comprehensive Income (Loss) | Accumulated Deficit | Treasury Stock | Deferred Compensation Obligation | Total Stockholders' Equity | Common Stock | | Additional Paid-In Capital | Accumulated Other Comprehensive Income (Loss) | Accu D |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | | | | | | | Shares | Amount | | | |
| Balance as of December 31, 2023 | 82,315,590 | $ 82 | $ 3,662,346 | $ 647 | $ (3,387,661) | $ (432) | $ 432 | $ 275,414 | | | | | |
| Balance as of March 31, 2024 | 83,094,037 | $ 83 | $ 3,698,957 | $ (431) | $ (3,558,345) | $ (3,332) | $ 3,332 | $ 140,264 | | | | | |
| Issuance of common stock and pre-funded warrants in connection with the underwritten public offering, net | 8,782,051 | 9 | 380,857 | — | — | — | — | 380,866 | | | | | |
| Stock-based compensation | | — | 36,671 | — | — | — | — | 36,671 | — | — | 39,476 | — | |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Issuance of common stock under equity plan awards, net of tax | 778,447 | 1 | (60) | — | — | — | — | (59) | 259,296 | — | 4,074 | — | |
| Deferred compensation | — | — | — | — | — | (2,900) | 2,900 | — | — | — | — | — | |
| Other comprehensive loss | — | — | — | (1,078) | — | — | — | (1,078) | — | — | — | (664) | |
| Net loss | — | — | — | — | (170,684) | — | — | (170,684) | — | — | — | — | (1 |
| Balance as of March 31, 2024 | 83,094,037 | $ 83 | $ 3,698,957 | $ (431) | $ (3,558,345) | $ (3,332) | $ 3,332 | $ 140,264 | | | | | |
| Balance as of June 30, 2024 | 92,135,384 | $ 92 | $ 4,123,364 | $ (1,095) | $ (3,689,943) | $ (3,395) | $ 3,395 | $ 432,418 | | | | | |

| | Common Stock | | Additional Paid-In Capital | Accumulated Other Comprehensive Income (Loss) | Accumulated Deficit | Treasury Stock | Deferred Compensation Obligation | Total Stockholders' Equity | Common Stock | | Additional Paid-In Capital | Accumulated Other Comprehensive Income (Loss) | Ac |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | | | | | | | Shares | Amount | | | |
| Balance as of December 31, 2022 | 70,197,297 | $ 70 | $ 3,140,019 | $ (6,573) | $ (2,781,022) | $ — | $ — | $ 352,494 | | | | | |
| Balance as of December 31, 2023 | 82,315,590 | $ 82 | $ 3,662,346 | $ 647 | $ (3,387,661) | $ (432) | $ 432 | $ 275,414 | | | | | |
| Issuance of common stock and pre-funded warrants in connection with the underwritten public offering, net | 8,782,051 | 9 | 380,857 | — | — | — | — | 380,866 | | | | | |
| Stock-based compensation | — | — | 30,103 | — | — | — | — | 30,103 | — | — | 76,147 | — | |
| Issuance of common stock under equity plan awards, net of tax | 462,952 | 1 | (751) | — | — | — | — | (750) | 1,037,743 | 1 | 4,014 | — | |
| Deferred compensation | — | — | — | — | — | (356) | 356 | | — | — | — | — | |
| Other comprehensive income | — | — | — | 2,606 | — | — | — | 2,606 | | | | | |
| Other comprehensive loss | — | — | — | (1,742) | — | — | — | (1,742) | | | | | |
| Net loss | — | — | — | — | (163,972) | — | — | (163,972) | — | — | — | — | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Balance as of March 31, 2023 | 70,660,249 | $ 71 | $ 3,169,371 | $ (3,967) | $ (2,944,994) | $ (356) | $ 356 | $ 220,481 |
| Balance as of June 30, 2024 | 92,135,384 | $ 92 | $ 4,123,364 | $ (1,095) | $ (3,689,943) | $ (3,395) | $ 3,395 | $ 432,418 |



| | Common Stock | | Additional Paid-In | Accumulated Other Comprehensive | Accumulated | Treasury | Deferred Compensation | Total Stockholders' |
|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | Capital | Income (Loss) | Deficit | Stock | Obligation | Equity |
| Balance as of March 31, 2023 | 70,660,249 | $ 71 | $ 3,169,371 | $ (3,967) | $ (2,944,994) | $ (356) | $ 356 | $ 220,481 |
| Issuance of common stock in connection with at-the-market offering, net | 564,302 | — | 28,507 | — | — | — | — | 28,507 |
| Stock-based compensation | — | — | 34,432 | — | — | — | — | 34,432 |
| Issuance of common stock under equity plan awards, net of tax | 240,873 | — | 4,569 | — | — | — | — | 4,569 |
| Deferred compensation | — | — | — | — | — | (25) | 25 | — |
| Other comprehensive income | — | — | — | 869 | — | — | — | 869 |
| Net loss | — | — | — | — | (159,828) | — | — | (159,828) |
| Balance as of June 30, 2023 | 71,465,424 | $ 71 | $ 3,236,879 | $ (3,098) | $ (3,104,822) | $ (381) | $ 381 | $ 129,030 |

| | Common Stock | | Additional Paid-In | Accumulated Other Comprehensive | Accumulated | Treasury | Deferred Compensation | Total Stockholders' |
|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | Capital | Income (Loss) | Deficit | Stock | Obligation | Equity |
| Balance as of December 31, 2022 | 70,197,297 | $ 70 | $ 3,140,019 | $ (6,573) | $ (2,781,022) | $ — | $ — | $ 352,494 |
| Issuance of common stock in connection with at-the-market offering, net | 564,302 | — | 28,507 | — | — | — | — | 28,507 |
| Stock-based compensation | — | — | 64,535 | — | — | — | — | 64,535 |
| Issuance of common stock under equity plan awards, net of tax | 703,825 | 1 | 3,818 | — | — | — | — | 3,819 |
| Deferred compensation | — | — | — | — | — | (381) | 381 | — |
| Other comprehensive income | — | — | — | 3,475 | — | — | — | 3,475 |
| Net loss | — | — | — | — | (323,800) | — | — | (323,800) |
| Balance as of June 30, 2023 | 71,465,424 | $ 71 | $ 3,236,879 | $ (3,098) | $ (3,104,822) | $ (381) | $ 381 | $ 129,030 |

See accompanying notes.



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

| | Three Months Ended March 31, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2024 | 2023 | 2024 | 2023 |
| **Operating activities:** | | | | |
| Net loss | $ (170,684) | $ (163,972) | $ (302,282) | $ (323,800) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | | |
| Stock-based compensation | 36,926 | 31,952 | 76,297 | 66,606 |
| Amortization of discount on marketable debt securities, net | (3,756) | (2,994) | (6,703) | (6,213) |
| Depreciation and amortization | 8,845 | 5,236 | 17,707 | 10,597 |
| Change in fair value of equity investments | (3,746) | 334 | 245 | 73 |
| Non-cash royalty revenue | (18,063) | (4,882) | (44,352) | (22,152) |
| Non-cash interest expense on liabilities for sales of future royalties | 15,847 | 15,636 | 31,807 | 31,011 |
| Other | (77) | 187 | (748) | 2,055 |
| Changes in operating assets and liabilities: | | | | |
| Accounts receivable | (24,908) | (2,508) | (22,750) | (17,586) |
| Inventory | (2,124) | 150 | (6,251) | (1,507) |
| Other assets | 6,553 | (519) | (449) | 11,594 |
| Accounts payable, accrued, and other liabilities | (35,540) | (35,487) | (10,211) | (23,706) |
| Net cash used in operating activities | (190,727) | (156,867) | (267,690) | (273,028) |
| **Investing activities:** | | | | |
| Purchase of property, plant, and equipment | (3,211) | (25,034) | (5,220) | (38,972) |
| Purchase of marketable debt securities | (21,928) | (62,024) | (25,301) | (165,305) |
| Proceeds from sale of marketable debt securities | 2,845 | 10,715 | 3,022 | 14,627 |
| Proceeds from maturities of marketable debt securities | 128,794 | 191,598 | 197,104 | 407,221 |
| Payment for intangible asset | (10,000) | — | | |
| Payments for intangible asset | (12,500) | (2,500) | | |
| Other | (2,065) | (3,951) | (2,106) | (4,349) |
| Net cash provided by investing activities | 94,435 | 111,304 | 154,999 | 210,722 |
| **Financing activities:** | | | | |
| Proceeds from the issuance of common stock and pre-funded warrants in connection with the underwritten public offering, net | 380,866 | — | | |
| Proceeds from the issuance of common stock in connection with at-the-market offering, net | — | 28,507 | | |
| Proceeds from the issuance of common stock under equity plan awards, net of tax | (58) | (750) | 4,015 | 3,819 |
| Other | — | 28 | — | (28) |
| Net cash used in financing activities | (58) | (722) | | |
| Net cash provided by financing activities | 384,881 | 32,298 | | |
| Effect of exchange rate changes on cash | (679) | 211 | (1,327) | 75 |
| Net decrease in cash, cash equivalents and restricted cash | (97,029) | (46,074) | | |
| Net increase (decrease) in cash, cash equivalents and restricted cash | 270,863 | (29,933) | | |
| Cash, cash equivalents and restricted cash at beginning of period | 219,399 | 137,601 | 219,399 | 137,601 |
| Cash, cash equivalents and restricted cash at end of period | $ 122,370 | $ 91,527 | $ 490,262 | $ 107,668 |
| | | | | |
| **Supplemental disclosures of non-cash information:** | | | | |
| Stock-based compensation capitalized into ending inventory | $ 2,786 | $ 2,276 | $ 3,004 | $ 2,303 |
| Costs of property, plant and equipment included in accounts payable, accrued, and other liabilities | $ 1,280 | $ 9,137 | $ 899 | $ 6,063 |
| Non-cash interest expense on liabilities for sales of future royalties capitalized during the year into ending property, plant and equipment | $ — | $ 3,820 | $ — | $ 7,969 |

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 ultrarare genetic diseases. The Company operates as one reportable segment and has four commercially approved products.

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

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

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

Evkeeza® (evinacumab) is approved in the U.S. and the European Economic Area, or EEA, for the treatment of homozygous familial hypercholesterolemia, or HoFH. The Company has exclusive rights to commercialize Evkeeza® (evinacumab) outside of the U.S. 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 st 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 comm urea cycle disorder;
- UX143 (setrusumab), which is subject to the Company's collaboration agreement with Mereo BioPharma 3, or Mereo, is a fully human monoclonal antibody that inhibits sclerostin, a protein that acts on a key bone-signaling pathway and inhibits the activity of bone-forming cells for the treatment of patients with osteogenesis imperfect, 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 maternally inherited allele of the UBE3A gene.; 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 single intravenous infusion to improve copper distribution and excretion from the body and reverse pathological findings of Wilson liver disease; disease.

The Company has sustained operating losses and expects such annual losses to continue over the next several years. The Company's ultimate success depends on the outcome of its research and development and commercialization activities. Through March 31, 2024 June 30, 2024, the Company has relied primarily on its sale of equity securities, its revenues from commercial products, its sale of future royalties, and strategic collaboration arrangements to finance its operations. The Company may need to raise additional capital to fully implement its business plans through the issuance of equity, borrowings, or strategic alliances with partner companies. However, if such financing is not available at adequate levels, the Company would need to reevaluate its operating plans.

## 2. Summary of Significant Accounting Policies

### Basis of Presentation

The accompanying unaudited Condensed Consolidated Financial Statements include the accounts of the Company and its wholly-owned subsidiaries and 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. 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 21, 2024, or Annual Report, with the United States Securities and Exchange Commission, or the SEC.

The results of operations for the three and six months ended March 31, 2024 June 30, 2024 are not necessarily indicative of the results to be expected for the year ending December 31, 2024. The Condensed Consolidated Balance Sheet as of December 31, 2023 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.

**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, | | June 30, | |
|---|---|---|---|---|
| | 2024 | 2023 | 2024 | 2023 |
| Cash and cash equivalents | $ 112,250 | $ 85,768 | $ 480,693 | $ 102,059 |
| Restricted cash included in other current assets | 6,304 | 1,964 | 6,172 | 1,696 |
| Restricted cash included in other non-current assets | 3,816 | 3,795 | 3,397 | 3,913 |
| Total cash, cash equivalents, and restricted cash shown in the statements of cash flows | $ 122,370 | $ 91,527 | $ 490,262 | $ 107,668 |

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

The Company's expected loss allowance methodology for the receivables is developed using historical collection experience, current and future economic market conditions, a review of the current aging status and financial condition of the entities. Specific allowance amounts are established to record the appropriate allowance for customers that have a higher probability of default. Balances are written off when determined to be uncollectible. The Company's expected loss allowance methodology for the debt securities is developed by reviewing the extent of the unrealized loss, the size, term, geographical location, and industry of the issuer, the issuers' credit ratings and any changes in those ratings, as well as reviewing current and future economic market conditions and the issuers' current status and financial condition. There were no material credit losses recorded for receivables and available-for-sale debt securities which were attributable to credit risk for the three and six months ended March 31, 2024 June 30, 2024 and 2023.



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**Revenue Recognition**

*Product Sales*

The Company sells its approved products through a limited number of distributors. Under ASC 606, revenue from product sales is recognized at the point in time when 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 Accounting Standards Codification, or ASC, 808, *Collaborative Agreements*, which provides guidance on the presentation and disclosure of collaborative arrangements. Generally, the classification of the transactions under the collaborative arrangements is determined based on the nature of contractual terms of the arrangement, along with the nature of the operations of the participants. The Company records its share of collaboration revenue, net of transfer pricing related to net sales in the period in which such sales occur, if the Company is considered as an agent in the arrangement. The Company is considered an agent when the collaboration partner controls the product before transfer to the customers and has the ability to direct the use of and obtain substantially all of the remaining benefits from the product. Funding received related to research and development services and commercialization costs is generally classified as a reduction of research and development expenses and selling, general and administrative expenses, respectively, in the 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 licensing of intellectual property.

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 records the royalty revenue from the net sales of Crysvita in the applicable territories on a prospective basis as non-cash royalty revenue in the 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, or* ASC 606, to determine the distinct performance obligations. The Company analogizes to ASC 606 for the accounting for distinct performance obligations for which there is a customer relationship. Prior to recognizing revenue, the Company makes estimates of the transaction price, including variable consideration that is subject to a constraint. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur and when the uncertainty associated with the variable consideration is subsequently resolved. Total consideration may include nonrefundable upfront license fees, payments for research and development activities, reimbursement of certain third-party costs, payments based upon the achievement of specified milestones, and royalty payments based on product sales derived from the collaboration.

If there are multiple distinct performance obligations, the Company allocates the transaction price to each distinct performance obligation based on its relative standalone selling price. The standalone selling price is generally determined based on the prices charged to customers or using expected cost-plus margin. The Company estimates the efforts needed to complete the



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performance obligations and recognizes revenue by measuring the progress towards complete satisfaction of the performance obligations using input measures.

**Deferred Compensation Plan**

The Company maintains a nonqualified deferred compensation plan whereby certain employees and members of the board of directors are able to defer certain equity awards and other compensation. Amounts deferred are invested into shares of the Company's common stock, mutual funds, and other investment options. The plan complies with the provisions of Section 409A of the Internal Revenue Code. All of the various mutual funds held in the plan are classified as trading securities and recorded at fair value in other non-current assets in the Condensed Consolidated Balance Sheets with changes in fair value recognized as earnings in the period they occur. The short-term portion of the corresponding liability for the plan is included in accrued expenses. The long-term portion of the liability is included in other non-current liabilities in the Condensed Consolidated Balance Sheets. Certain equity awards deferred under the plan are required to be settled through the issuance of Company stock. These awards are recorded as treasury stock and deferred compensation obligation within stockholders' equity.

**3. Financial Instruments**

Financial assets and liabilities are recorded at fair value. The carrying amount of certain financial instruments, including cash and cash equivalents, accounts receivable, accounts payable and accrued liabilities, approximate fair value due to their relatively short maturities. Assets and liabilities recorded at fair value on a recurring basis in the balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value is defined as the exchange price that would be received for an asset or an exit price that would be paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

*Level 1*—Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

*Level 2*—Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

*Level 3*—Unobservable inputs that are significant to the measurement of the fair value of the assets or liabilities that are supported by little or no market data.

The Company 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, 2024 | | | | June 30, 2024 | | | |
|---|---|---|---|---|---|---|---|---|
| | Level 1 | Level 2 | Level 3 | Total | Level 1 | Level 2 | Level 3 | Total |
| **Financial Assets:** | | | | | | | | |
| Money market funds | $ 51,029 | $ — | $ — | $ 51,029 | $ 427,247 | $ — | $ — | $ 427,247 |
| Certificates of deposit and time deposits | — | 17,986 | — | 17,986 | — | 15,986 | — | 15,986 |
| Corporate bonds | — | 179,819 | — | 179,819 | — | 169,365 | — | 169,365 |
| Commercial paper | — | 21,966 | — | 21,966 | — | 12,226 | — | 12,226 |
| Asset-backed securities | — | 546 | — | 546 | — | 369 | — | 369 |
| U.S. Government Treasury and agency securities | 58,539 | 206,809 | — | 265,348 | 30,732 | 176,728 | — | 207,460 |
| Investment in Solid common stock | 6,950 | — | — | 6,950 | 2,959 | — | — | 2,959 |
| Deferred compensation assets | — | 13,105 | — | 13,105 | — | 13,712 | — | 13,712 |
| Total financial assets | $ 116,518 | $ 440,231 | $ — | $ 556,749 | $ 460,938 | $ 388,386 | $ — | $ 849,324 |
| **Financial Liabilities:** | | | | | | | | |
| Deferred compensation liabilities | $ — | $ 13,310 | $ — | $ 13,310 | $ — | $ 13,959 | $ — | $ 13,959 |

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

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

**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, 2024 | | | | June 30, 2024 | | | |
|---|---|---|---|---|---|---|---|---|
| | | Gross Unrealized | | | | Gross Unrealized | | |
| | Amortized Cost | Gains | Losses | Estimated Fair Value | Amortized Cost | Gains | Losses | Estimated Fair Value |
| Money market funds | $ 51,029 | $ — | $ — | $ 51,029 | $ 427,247 | $ — | $ — | $ 427,247 |
| Certificates of deposit and time deposits | 17,986 | — | — | 17,986 | 15,986 | — | — | 15,986 |
| Corporate bonds | 179,694 | 331 | (206) | 179,819 | 169,414 | 139 | (188) | 169,365 |
| Commercial paper | 21,966 | — | — | 21,966 | 12,226 | — | — | 12,226 |
| Asset-backed securities | 547 | — | (1) | 546 | 369 | — | — | 369 |
| U.S. Government Treasury and agency securities | 265,426 | 91 | (169) | 265,348 | 207,810 | 1 | (351) | 207,460 |
| Total | $ 536,648 | $ 422 | $ (376) | $ 536,694 | $ 833,052 | $ 140 | $ (539) | $ 832,653 |

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

At March 31, 2024 June 30, 2024, the remaining contractual maturities of available-for-sale securities were less than three years. There have been no significant realized gains or losses on available-for-sale securities for the periods presented.

**Inventory**

Inventory consists of the following (in thousands):

| | March 31, 2024 | December 31, 2023 | June 30, 2024 | December 31, 2023 |
|---|---|---|---|---|
| Work-in-process | $ 22,822 | $ 18,859 | $ 25,252 | $ 18,859 |
| Finished goods | 13,085 | 15,110 | 14,885 | 15,110 |
| Total inventory | $ 35,907 | $ 33,969 | $ 40,137 | $ 33,969 |

**Accrued Liabilities**

Accrued liabilities consist of the following (in thousands):

| | March 31, 2024 | December 31, 2023 | June 30, 2024 | December 31, 2023 |
|---|---|---|---|---|
| Research, clinical study, and manufacturing expenses | $ 47,703 | $ 65,326 | $ 36,325 | $ 65,326 |
| Payroll and related expenses | 51,216 | 82,936 | 61,052 | 82,936 |
| Revenue related reserves | 27,972 | 17,029 | | |
| Other | 50,214 | 48,224 | 29,072 | 31,195 |
| Total accrued liabilities | $ 149,133 | $ 196,486 | $ 154,421 | $ 196,486 |



**5. Revenue**

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

| | Three Months Ended March 31, | | Three Months Ended June 30, | | Six Months Ended June 30, | |
|---|---|---|---|---|---|---|
| | 2024 | 2023 | 2024 | 2023 | 2024 | 2023 |
| Product sales: | | | | | | |
| Crysvita | $ 36,241 | $ 21,234 | $ 40,449 | $ 16,884 | $ 76,690 | $ 38,118 |
| Mepsevii | 6,611 | 8,480 | 6,145 | 8,439 | 12,756 | 16,919 |
| Dojolvi | 16,362 | 14,303 | 19,355 | 16,491 | 35,717 | 30,794 |
| Evkeeza | 3,275 | 212 | 7,856 | 365 | 11,131 | 577 |
| Total product sales | 62,489 | 44,229 | 73,805 | 42,179 | 136,294 | 86,408 |
| Crysvita royalty revenue | 46,344 | 4,882 | 73,221 | 46,331 | 119,565 | 51,213 |
| Collaboration and license revenue: | | | | | | |
| Crysvita collaboration revenue in Profit-Share Territory | — | 49,906 | — | 19,799 | — | 69,705 |
| Daiichi Sankyo | — | 1,479 | — | — | — | 1,479 |
| Total collaboration and license revenue | — | 51,385 | — | 19,799 | — | 71,184 |
| Total revenues | $ 108,833 | $ 100,496 | $ 147,026 | $ 108,309 | $ 255,859 | $ 208,805 |

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

| | Three Months Ended March 31, | | Three Months Ended June 30, | | Six Months Ended June 30, | |
|---|---|---|---|---|---|---|
| | 2024 | 2023 | 2024 | 2023 | 2024 | 2023 |

| | | | | | | |
|---|---|---|---|---|---|---|
| North America | $ 57,682 | $ 67,132 | $ 88,889 | $ 79,289 | $ 146,571 | $ 146,421 |
| Latin America | 35,178 | 22,799 | 38,929 | 19,068 | 74,107 | 41,867 |
| Europe | 15,973 | 9,387 | | | | |
| Japan | — | 1,178 | | | | |
| Europe, Middle East, and Africa, or EMEA | 16,157 | 9,952 | 32,130 | 19,339 | | |
| Asia-Pacific, or APAC | 3,051 | — | 3,051 | 1,178 | | |
| Total revenues | $ 108,833 | $ 100,496 | $ 147,026 | $ 108,309 | $ 255,859 | $ 208,805 |

The Company's largest accounts receivable balance was from a collaboration partner and accounted for 42 63% and 53% of the total accounts receivable balance as of March 31, 2024 June 30, 2024 and December 31, 2023, respectively. A separate customer accounted for 20 12% and 8 2%, respectively, of the total accounts receivable balance as of March 31, 2024 June 30, 2024 and December 31, 2023, respectively.



**6. GeneTx Acquisition**

In August 2019, the Company entered into a Program Agreement and a Unitholder Option Agreement with GeneTx Biotherapeutics LLC, or GeneTx, to collaborate on the development of GeneTx's GTX-102, an ASO for the treatment of Angelman syndrome. In July 2022, pursuant to the terms of the Unitholder Option Agreement, as amended, the Company exercised the option to acquire GeneTx and entered into a Unit Purchase Agreement, or the Purchase Agreement, pursuant to which the Company purchased all the outstanding units of GeneTx. In accordance with the terms of the Purchase Agreement, the Company paid the option exercise price of $75.0 million and an additional $15.6 million to acquire the outstanding cash of GeneTx, and adjustments for working capital and transaction expenses of $0.6 million, for a total purchase consideration of $91.2 million. The Company may be required to make payments of up to $190.0 million upon the achievement of certain milestones, including up to $30.0 million in milestone payments upon achievement of the earlier of initiation of a Phase 3 clinical study or product approvals in Canada and the U.K., up to $85.0 million in additional regulatory approval milestones for the achievement of U.S. and EU product approvals, and up to $75.0 million in commercial milestone payments based on annual worldwide net product sales. The Company will also pay tiered mid- to high single-digit percentage royalties based on licensed product annual net sales. If the Company receives and resells an FDA priority review voucher, or PRV, in connection with a new drug application approval, GeneTx is entitled to receive a portion of proceeds from the sale or a cash payment from the Company if the Company choses to retain the PRV. As part of the Company's acquisition of GeneTx, the Company assumed a License Agreement with Texas A&M University, or TAMU. Under this agreement, TAMU is eligible to receive from the Company up to $23.5 million upon the achievement of various future milestones, a nominal annual license fee that may increase up to a maximum of $2.0 million, as well as royalties in the mid-single-digits of net sales.

The transaction was accounted as an asset acquisition, as substantially all of the fair value of the gross assets acquired was concentrated in a single identifiable in-process research and development intangible asset. Prior to the achievement of certain



development and regulatory milestones, the acquired in-process research and development intangible asset has not yet reached technological feasibility and has no alternative future use. Accordingly, to date, amounts paid to GeneTx, net of cash and working capital acquired, were classified as in-process research and development expense.

**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.

*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.

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

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

The Company and KKC shared commercial responsibilities and profits in the Profit-Share Territory until April 2023. Under the collaboration agreement, KKC manufactured and supplied Crysvita for commercial use in the Profit-Share Territory and charged the Company a transfer price of 30% of net sales in 2023, and 35% prior to December 31, 2022. The remaining profit or loss after supply costs from commercializing products in the Profit-Share Territory was shared between the Company and KKC on a 50/50 basis until April 2023. In April 2023, commercialization responsibilities for Crysvita in the Profit-Share Territory transitioned to KKC. Thereafter, the Company is entitled to receive a tiered double-digit revenue share from the mid-20% range up to a maximum rate of 30%.

In 2022, the Company entered into an amendment to the collaboration agreement which granted the Company the right to continue to support KKC in commercial field activities in the U.S. through April 2024, subject to the limitations and conditions set forth in the amendment. The parties subsequently mutually agreed to extend the Company's right to continue to support KKC in



commercial field activities in the U.S. through December 31, 2024, and as a result, the Company will continue to support commercial field efforts in the U.S. through a cost share arrangement through December 2024. After December 31, 2024, the Company's rights to promote Crysvita in the U.S. will be limited to medical geneticists and the Company will solely bear its expenses for the promotion of Crysvita in the Profit-Share Territory.

As KKC was the principal in the sale transaction with the customer during the profit-share period, the Company recognized a pro-rata share of collaboration revenue, net of transfer pricing, in the period the sale occurs. 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 the royalty revenue as 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. The Company records this revenue as royalty revenue.

*Product Sales Revenue for Other Territories*

The Company is responsible for commercializing Crysvita in Latin America and Turkey. The Company is considered the principal in these territories as the Company controls the product before it is transferred to the customer. Accordingly, the Company records revenue on a gross basis for the sale of Crysvita once the product is delivered and the risk and title of the product is transferred to the distributor. KKC has the option to assume responsibility for commercialization efforts in Turkey from the Company, after a certain minimum period.



Under the collaboration agreement, KKC manufactures and supplies Crysvita, which is purchased by the Company for sales in Latin American territories and charges the Company a transfer price of 30% of net sales. The transfer price on these sales was 35% prior to December 31, 2022. The Company also pays to KKC a low single-digit royalty on net sales in Latin America.

Total Crysvita revenue was as follows (in thousands):

| | Three Months Ended March 31, | |
|---|---|---|
| | 2024 | 2023 |
| Revenue in Profit-Share Territory: | | |
| Royalty revenue | $ 28,281 | $ — |
| Non-cash royalty revenue | 12,121 | — |
| Collaboration revenue | — | 49,906 |
| Total revenue in Profit-Share Territory | 40,402 | 49,906 |
| Product sales | 36,241 | 21,234 |
| Non-cash royalty revenue in European Territories | 5,942 | 4,882 |

| | | |
|---|---|---|
| Total Crysvita revenue | $ 82,585 | $ 76,022 |

*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. 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

Total Crysvita revenue was as royalty revenue. follows (in thousands):

| | Three Months Ended June 30, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2024 | 2023 | 2024 | 2023 |
| Revenue in Profit-Share Territory: | | | | |
| Royalty revenue | $ 46,932 | $ 29,061 | $ 75,213 | $ 29,061 |
| Non-cash royalty revenue | 20,113 | 12,454 | 32,234 | 12,454 |
| Collaboration revenue | — | 19,799 | — | 69,705 |
| Total revenue in Profit-Share Territory | 67,045 | 61,314 | 107,447 | 111,220 |
| Product sales | 40,449 | 16,884 | 76,690 | 38,118 |
| Non-cash royalty revenue in European Territories | 6,176 | 4,816 | 12,118 | 9,698 |
| Total Crysvita revenue | $ 113,670 | $ 83,014 | $ 196,255 | $ 159,036 |

*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. Additionally, KKC is owed a transfer price fee and royalties on certain revenues and the Company recorded amounts owed to KKC 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, | |
|---|---|---|
| | 2024 | 2023 |
| Research and development | $ 893 | $ 2,272 |
| Selling, general and administrative | 1,262 | 9,080 |
| Cost of sales | 11,077 | 5,542 |



| | Three Months Ended June 30, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2024 | 2023 | 2024 | 2023 |
| Research and development | $ (1,045) | $ (1,453) | $ (1,938) | $ (3,725) |
| Selling, general and administrative | (1,024) | (4,206) | (2,286) | (13,286) |
| Cost of sales | 12,626 | 3,986 | 23,703 | 9,528 |

*Collaboration Receivable and Payable*

The Company had accounts receivable from KKC in the amount of $42.4 67.2 million and $39.2 million from profit-share revenue and royalties and other receivables recorded in other current assets of $0.2 2.3 million and $1.1 million and accrued liabilities of $11.5 12.9 million and $5.3 million from inventory, commercial, and development activity reimbursements, as of March 31, 2024 June 30, 2024 and December 31, 2023, 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, the Company leads future global development of setrusumab in both pediatric and adult patients with Osteogenesis Imperfecta, or OI. The Company was granted an exclusive license to develop and commercialize setrusumab in the U.S., Turkey, and the rest of the world, excluding the European Economic Area, United Kingdom, and Switzerland, or the Mereo Territory, where Mereo retains commercial rights. Each party is responsible for post-marketing commitments and commercial supply in their respective territories.

Upon the closing of the transactions under the License and Collaboration Agreement with Mereo in January 2021, the Company made a payment of $50.0 million to Mereo. In July 2023, the Company made a $9.0 million payment to Mereo upon the achievement of a clinical milestone. Going forward, the Company may be required to make payments of up to $245.0 million upon the achievement of certain clinical, regulatory, and commercial milestones. The Company will pay for all global development costs as well as tiered double-digit percentage royalties to Mereo on net sales in the U.S., Turkey, and the rest of the world, and Mereo will pay the Company a fixed double-digit percentage royalty on net sales in the Mereo Territory.

Although Mereo is a variable interest entity, the Company is not the primary beneficiary as it does not have the power to direct the activities that would most significantly impact the economic performance of Mereo. Prior to the achievement of certain development milestones, all consideration paid to Mereo represents rights to potential future benefits associated with Mereo's in-process research and development activities, which have not reached technological feasibility and have no alternative future use.

**Regeneron**

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

The collaboration agreement is within the scope of ASC 808 which provides guidance on the presentation and disclosure of collaborative arrangements. As the Company would be the principal in future sale transactions with the customer, the Company 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.

The Company paid Regeneron a $30.0 million upfront payment upon the closing of the transaction in January 2022, and a $10.0 million regulatory milestone payment in January 2024, and a $2.5 million regulatory milestone payment in May 2024. As these payments are for the Company's use of intellectual property for Evkeeza for HoFH, they were recorded as intangible assets.

Under the collaboration agreement, the Company was reimbursed by Regeneron for development costs of $0.6 3.3 million and $3.2 2.8 million, net, for the three and six months ended March 31, 2024 June 30, 2024, respectively, recorded as offsets to research and 2023, development expense on the Condensed Consolidated Statements of Operations. The Company paid Regeneron $1.8 million and $5.0 million under this agreement for the three and six months ended June 30, 2023, respectively, recorded as research and development expense on the Condensed Consolidated Statements of Operations. The Company had collaboration receivables for this arrangement included in other current assets on the Condensed Consolidated Balance Sheets of $2.4 million and nil, and collaboration payables for this arrangement included in accrued liabilities on the Condensed Consolidated Balance Sheets of $1.2 1.0 million and $10.6 million as of March 31, 2024 June 30, 2024 and December 31, 2023, respectively. Additionally, Regeneron is owed a transfer price fee and royalties on certain revenues and the



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Company recorded amounts owed to Regeneron of $0.6 2.0 million and a $nominal 2.8 amount million was recorded in cost of sales on the Condensed Consolidated Statements of Operations for the three and six months ended March 31, 2024 June 30, 2024, respectively, and 2023, respectively. $0.1 million for the three and six months ended June 30, 2023.

**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 and six months ended March 31, 2024 June 30, 2024 as



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compared to those disclosed in "Note 8. 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 Condensed Consolidated Statements of Operations 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 of occurrence.

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 investments investment in the common stock of Solid were as follows (in thousands):

| | Common stock | Common stock |
|---|---|---|
| As of December 31, 2022 | $ 2,807 | $ 2,807 |
| Change in fair value | 397 | 397 |
| December 31, 2023 | 3,204 | |
| As of December 31, 2023 | 3,204 | |
| Change in fair value | 3,746 | (245) |
| March 31, 2024 | $ 6,950 | |
| As of June 30, 2024 | $ 2,959 | |

**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, 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), over the $314.2 million and $491.0 million, respectively, of net proceeds, is recorded as non-cash interest expense over the life of the arrangements. Consequently, the Company estimates an imputed interest on the unamortized portion of the liabilities and records interest expense relating to the transactions. The Company records the royalty revenue arising from the net sales of Crysvita in the applicable territories as 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, 2024 June 30, 2024 have been $79.3 85.5 million and $60.7 80.8 million, respectively.

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



amortization of the liabilities and the effective interest rate. The Company's effective annual interest rates were 6.2% and 7.8 7.7%, for RPI and OMERS, respectively, as of March 31, 2024 June 30, 2024.

There are a number of factors that could materially affect the amount and timing of royalty payments from KKC in the applicable territories, most of which are not within the Company's control. Such factors include, but are not limited to, the success of KKC's sales and promotion of Crysvita, changing standards of care, macroeconomic and inflationary pressures, the introduction of

competing products, pricing for reimbursement in various territories, manufacturing or other delays, intellectual property matters, adverse events that result in governmental health authority imposed restrictions on the use of Crysvita, significant changes in foreign exchange rates as the royalty payments are made in U.S. dollars, or USD, while significant portions of the underlying sales of Crysvita are made in currencies other than USD, and other events or circumstances that could result in reduced royalty payments from sales of Crysvita, all of which would result in a reduction of royalty revenue and the non-cash interest expense over the life of the arrangement. Conversely, if sales of Crysvita in the relevant territories are more than expected, the royalty revenue and the non-cash interest expense recorded by the Company would be greater over the term of the arrangements.

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

| | Liabilities for Sales of Future Royalties | | | Liabilities for Sales of Future Royalties | | |
|---|---|---|---|---|---|---|
| | RPI | OMERS | Total | RPI | OMERS | Total |
| December 31, 2022 | $ 365,189 | $ 510,250 | $ 875,439 | $ 365,189 | $ 510,250 | $ 875,439 |
| Royalty revenue | (20,783) | (38,524) | (59,307) | (20,783) | (38,524) | (59,307) |
| Non-cash interest expense | 32,235 | 43,200 | 75,435 | 32,235 | 43,200 | 75,435 |
| December 31, 2023 | 376,641 | 514,926 | 891,567 | 376,641 | 514,926 | 891,567 |
| Royalty revenue | (5,942) | (10,058) | (16,000) | (12,118) | (22,178) | (34,296) |
| Non-cash interest expense | 5,899 | 9,948 | 15,847 | 11,915 | 19,892 | 31,807 |
| March 31, 2024 | $ 376,598 | $ 514,816 | $ 891,414 | | | |
| June 30, 2024 | $ 376,438 | $ 512,640 | $ 889,078 | | | |

**9. Stock-Based Awards**

As of March 31, 2024 June 30, 2024, there were 1,398,838 1,711,846 shares available under the 2023 Incentive Plan, 6,694,377 6,567,545 shares available under the Amended & Restated 2014 Employee Stock Purchase Plan, and 115,324 23,673 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, | | Three Months Ended June 30, | | Six Months Ended June 30, | |
|---|---|---|---|---|---|---|
| | 2024 | 2023 | 2024 | 2023 | 2024 | 2023 |
| Cost of sales | $ 416 | $ 346 | $ 269 | $ 325 | $ 685 | $ 671 |
| Research and development | 20,541 | 18,120 | 21,674 | 19,138 | 42,215 | 37,258 |
| Selling, general and administrative | 15,977 | 13,473 | 17,420 | 15,190 | 33,397 | 28,663 |
| Total stock-based compensation expense | $ 36,934 | $ 31,939 | $ 39,363 | $ 34,653 | $ 76,297 | $ 66,592 |

**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, and 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 the weighted average 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, | | Three Months Ended June 30, | | Six Months Ended June 30, | |
|---|---|---|---|---|---|---|
| | 2024 | 2023 | 2024 | 2023 | 2024 | 2023 |
| Options to purchase common stock, restricted stock units, and performance stock units | 15,056,294 | 12,825,527 | 16,992,495 | 14,919,562 | 16,031,785 | 13,876,326 |
| Employee stock purchase plan | 110,146 | 97,917 | 24,405 | 23,966 | 12,002 | 12,049 |
| | 15,166,440 | 12,923,444 | 17,016,900 | 14,943,528 | 16,043,787 | 13,888,375 |

**11. Equity Transactions**

**At-the-Market Offerings**

In February 2024, the Company entered into a Sales Agreement with Cowen and Company, LLC, or Cowen, pursuant to which the Company may offer and sell shares of the Company's common stock having an aggregate offering proceeds up to $350.0 million, from time to time, in at-the-market, or ATM, offerings through Cowen. No shares were sold under this agreement during the three and six months ended March 31, 2024 June 30, 2024.

**Underwritten Public Offering**

In October 2023, the Company completed an underwritten public offering in which 9,833,334 shares of common stock were sold, including the exercise in full by the underwriters of their option to purchase an additional 1,500,000 shares, at a public offering price of $30.00 per share. In connection with the offering, the Company sold to certain investors pre-funded warrants, in lieu of common stock, to purchase 1,666,722 shares of common stock at a purchase price of $29.999 per pre-funded warrant, which equals the public offering price per share of common stock less the $0.001 exercise price per share of each pre-funded warrant. The total proceeds that the Company received from the offering were $326.5 million, net of underwriting discounts and commissions. As

In June 2024, the Company completed an underwritten public offering in which 8,782,051 shares of March 31, 2024, common stock were sold, including the exercise in full by the underwriters of their option to purchase an additional no 1,346,153ne shares, at a public offering price of $39.00 per share. In connection with the offering, the Company sold to certain investors pre-funded warrants, had been exercised. in lieu of common stock, to purchase 1,538,501 shares of common stock at a purchase price of $38.999 per pre-funded warrant, which equals the public offering price per share of common stock less the $0.001 exercise price per share of each pre-funded warrant. The total proceeds that the Company received from the offering were $380.9 million, net of underwriting discounts and commissions.

The pre-funded warrants were classified as a component of permanent equity in the Company's Condensed Consolidated Balance Sheets as they are freestanding financial instruments that are immediately exercisable, do not embody an obligation for the Company to repurchase its own shares and permit the holders to receive a fixed number of shares of common stock upon exercise. All of the shares underlying the pre-funded warrants have been included in the weighted-average number of shares of common stock used to calculate net loss per share, basic and diluted, attributable to common stockholders because the shares may be issued for little or no consideration, are fully vested, and are exercisable after the original issuance date of the pre-funded warrants. As of June 30, 2024, none of the pre-funded warrants had been exercised.

The table below summarizes the pre-funded warrants activity:

| | Pre-funded warrants |
|---|---|
| As of December 31, 2022 | — |
| Issuance of pre-funded warrants | 1,666,722 |
| As of December 31, 2023 | 1,666,722 |
| Issuance of pre-funded warrants | 1,538,501 |
| As of June 30, 2024 | 3,205,223 |

**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 and nil million as research and development expense for this agreement for the three and six months ended March 31, 2024 June 30, 2024, respectively, and 2023, respectively. $0.3 million for the three and six months ended June 30, 2023. A total of $0.8 million has been recorded as research and development expense for this agreement to date.

**13. Accumulated Other Comprehensive Income (Loss)**

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

| | March 31, 2024 | December 31, 2023 | June 30, 2024 | December 31, 2023 |
|---|---|---|---|---|
| Foreign currency translation adjustments | $ (477) | $ (606) | $ (696) | $ (606) |
| Unrealized gain on available-for-sale securities | 46 | 1,253 | | |
| Unrealized gain (loss) on available-for-sale securities | (399) | 1,253 | | |

| | | | | |
|---|---|---|---|---|
| Total accumulated other comprehensive income (loss) | $ (431) | $ 647 | $ (1,095) | $ 647 |



**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, 2023, 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 ultrarare genetic diseases. We have built a diverse portfolio of approved therapies and product candidates aimed at addressing diseases with high unmet medical need and clear biology for treatment, for which there are typically no approved therapies treating the underlying disease.

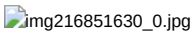
We were founded in April 2010 by our President and Chief Executive Officer, Emil Kakkis, M.D., Ph.D., and are led by a management team experienced in the development and commercialization of rare disease therapeutics. Our strategy is predicated upon time- and cost-efficient drug development, with the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

**Approved Products and Clinical Product Candidates**

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

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





**Approved Products**

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

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

***Mepsevii for the treatment of MPS VII***

Mepsevii is an enzyme replacement therapy administered intravenously, or IV, that replaces the missing enzyme (beta-glucuronidase), developed for the treatment of Mucopolysaccharidosis VII, also known as 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 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 long-chain fatty acid oxidation disorders, or 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 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 homozygous familial hypercholesterolemia, or 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, as a first-in-class therapy for use together with diet and other LDL-C lowering therapies 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 from the FDA, and was accepted into the EMA's Priority Medicines program, or PRIME, program. Setrusumab is subject to our collaboration agreement with Mereo and is the lead clinical asset in our bone endocrinology franchise.

***GTX-102 for the treatment of Angelman Syndrome***

GTX-102 is an antisense oligonucleotide, or ASO, administered by intrathecal injection (IT) 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 Priority Medicines program, or 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 break down 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 glycogen storage disease type Ia, or 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 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 ornithine transcarbamylase, or *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 more than 50,000 patients in the developed world. UX701 has received Orphan Drug Designation in the U.S. and in the EU. UX701 has received a Fast Track Designation from the FDA.

**Recent Program Updates**

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

In April June 2024, we announced all patients in the Phase 3 *Orbit* and *Cosmic* studies have been enrolled. The Phase 3 portion of *Orbit* enrolled 158 patients and is a randomized placebo-controlled study evaluating the effect of setrusumab compared to placebo on the rate of annualized clinical fractures in patients aged five to <25 years. *Cosmic* enrolled 66 patients and is an active-controlled study evaluating the effect of setrusumab compared to intravenous bisphosphonate (IV-BP) therapy on annualized total fracture rate in patients aged two to less than seven years. Additional longer-term safety and efficacy data positive 14-month results from the Phase 2 portion of the ongoing Phase 2/3 *Orbit* study are expected demonstrating that, as of a May 24, 2024 data cut-off date, treatment with setrusumab continued to show statistically significant reductions in the second half incidence of 2024. fractures in patients with OI. Treatment with setrusumab also resulted in ongoing and meaningful improvements in lumbar spine bone mineral density, or BMD, at month 12 without evidence of plateau.

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

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

More detailed 14-month data will be presented at a future scientific meeting.

***GTX-102 for the treatment of Angelman Syndrome***

In January July 2024, we announced that enrollment the completion of a successful End of Phase 2 meeting the FDA supporting our Phase 3 study plans for GTX-102. The pivotal *Aspire* Phase 3 study will be a global, randomized, double-blind, sham-controlled trial and will include a 48-week primary efficacy analysis period enrolling approximately 120 patients with Angelman syndrome with a genetically confirmed diagnosis of full maternal UBE3A gene deletion. The primary endpoint will be improvement in cognition assessed by Bayley-4 cognitive raw score. It will also include the Expansion Cohorts had been completed in key secondary endpoint of the Phase 1/2 Multi-domain Responder Index (MDRI) across all five domains of cognition, receptive communication, behavior, gross motor function, and sleep. Individual secondary endpoints were



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also discussed and aligned on with the FDA for the domains of communication, behavior, motor function and sleep. We also discussed with the FDA plans to initiate the *Aurora* study, an additional, open-label clinical study to evaluate the safety and efficacy of GTX-102 for the treatment of patients with other Angelman syndrome. Across the Phase 1/2,

including the Dose Escalation syndrome genotypes and Expansion Cohorts, there are a total of 74 patients enrolled in the Phase 1/2 study. The Expansion Cohorts will evaluate many of the same safety, pharmacokinetic, and efficacy measures as the previously enrolled Dose Escalation Cohorts plus some new evaluations. other age groups.

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

As previously reported and as of April 5, 2024, there were two patients who had mild or moderate lower extremity weakness across 53 patients who have completed the loading phase in the Expansion Cohorts A-E. Both were in Cohorts A & B and none reported in Cohorts C–E, as of the data cutoff. The lower extremity weakness resolved rapidly without sequelae and patients remain in the study without ongoing safety concerns and are expected to continue dosing. The FDA and other regulatory agencies were notified and raised no issues nor required additional actions. There were no other unexpected serious adverse events. We expect the pivotal Phase 3 *Aspire* study to share additional long-term safety start by the end of 2024 and efficacy data from the Phase 1/2 *Aurora* study and plan to continue to provide routine safety updates with efficacy updates. We currently expect to have an End of Phase 2 meeting with the FDA start in mid-2024 and with other regulatory agencies in the second half of 2024. 2025.



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

In February June 2024, we presented new announced that we reached agreement with the FDA that cerebral spinal fluid heparan sulfate is a reasonable surrogate endpoint that could support submission of a biologics license application, or BLA, seeking accelerated approval for UX111. As discussed with the FDA, the BLA filing will be based on the available data including from the ongoing pivotal *Transpher A* study evaluating the efficacy safety and safety efficacy of UX111 in children with MPS IIIA at the 20th Annual WORLD*Symposium*TM. IIIA. The presentation showed reductions details of HS exposure in cerebrospinal fluid correlated with improved long-term cognitive function in patients with MPS IIIA following treatment with UX111. Discussions a BLA will be finalized with the FDA seeking an accelerated review path are ongoing. in a pre-BLA meeting that is expected in the second half of 2024, with the intent to file our application late this year or early next year.

***DTX401 for the treatment of Glycogen Storage Disease Type Ia, or GSDIA***

In May 2023, 2024 we announced positive topline results from our Phase 3 *GlucoGene* study for the last patient had been dosed treatment of patients aged eight years and older. The study achieved its primary endpoint, demonstrating that treatment with DTX401 resulted in a statistically significant and clinically meaningful reduction in daily cornstarch intake compared with placebo at Week 48. The mean percent reduction was 41.3% in the DTX401 group (n=20) compared with 10.3% in the placebo group (n=24) at Week 48 ($p<0.0001$). Across patients treated with DTX401, the mean reduction in cornstarch continued to decline over the 48-week period. In the treatment group, all patients achieved a reduction in cornstarch, with 68% achieving ≥30% reduction and 37% achieving ≥50% reduction compared to the placebo group, which achieved the same reductions in 13% and 4% of patients, respectively, at Week 48. The study also successfully met key secondary endpoints of reduction in the number of cornstarch doses per day and maintenance of glucose control at Week 48.

Full 48 Week data from the Phase 3 study of DTX401. The 48-week Phase 3 study enrolled 49 patients eight years of age and older, randomized 1:1 will be presented at a scientific conference later this year. These results will be discussed with regulatory authorities to DTX401 (1.0 x 10^13 GC/kg dose) or placebo. The primary endpoint is the reduction support a marketing application in oral glucose replacement with cornstarch, while maintaining glucose control. We expect to share results from this Phase 3 study in the second quarter of 2024. 2025.

***DTX301 for the treatment of Ornithine Transcarbamylase, or OTC, deficiency***

We are currently randomizing and dosing patients in our 64-week Phase 3 study of DTX301. The patients in the study will be randomized 1:1 to DTX301 (1.7 x 10^13 GC/kg dose) or placebo. We plan to enroll approximately 50 patients 12 years of age and older. The co-primary endpoints are the percentage of patients who achieve a response, as measured by discontinuation or reduction in baseline disease management, and the 24-hour plasma ammonia levels. We expect to complete enrollment for the Phase 3 study in the second half of 2024.

***UX701 for the treatment of Wilson disease***

In February 2024, we announced that we have enrolled and dosed patients in the three dose escalating cohorts of the first, dose-finding, stage of the pivotal *Cyprus2*+ study of UX701 for the treatment of Wilson disease. During Stage 1, the safety and efficacy of UX701 is being evaluated across three, sequential dosing cohorts (Cohort 1: 5.0 x 10^12 GC/kg, Cohort 2: 1.0 x 10^13 GC/kg, and Cohort 3: 2.0 x 10^13 GC/kg) that will enable a dose to be selected for further evaluation in the second, randomized, placebo-controlled stage of this seamless pivotal study. Data from Stage 1 are expected in the second half of 2024 which will after the last patient has been on therapy for at least 6 months. This is expected to be followed by dose selection and initiation of Stage 2.

**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 loss was $170.7 million $131.6 million and $164.0 million $302.3 million for the three and six months ended March 31, 2024 June 30, 2024, respectively, and 2023, $159.8 million and $323.8 million for the three and six months ended June 30, 2023, respectively. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from selling, general and administrative costs associated with our operations.

Our total revenues were $108.8 million $147.0 million and $100.5 million $255.9 million for the three and six months ended March 31, 2024 June 30, 2024, respectively, and 2023, $108.3 million and $208.8 million for the three and six months ended June 30, 2023, respectively. The increase in revenue was largely driven by increases in demand for our approved products.



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As of March 31, 2024 June 30, 2024, we had $568.7 million $874.5 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, or GAAP. 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 and six months ended March 31, 2024 June 30, 2024, 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.



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**Results of Operations**

***Comparison of the three and six months ended March 31, 2024 June 30, 2024 to the three and six months ended March 31, 2023 June 30, 2023:***

*Revenue (dollars in thousands)*

| | Three Months Ended March 31, | | Dollar | % | Three Months Ended June 30, | | Dollar | % |
|---|---|---|---|---|---|---|---|---|
| | 2024 | 2023 | Change | Change | 2024 | 2023 | Change | Change |
| Product sales: | | | | | | | | |
| Crysvita | $ 36,241 | $ 21,234 | $ 15,007 | 71 % | $ 40,449 | $ 16,884 | $ 23,565 | 140 % |
| Mepsevii | 6,611 | 8,480 | (1,869) | -22 % | 6,145 | 8,439 | (2,294) | -27 % |
| Dojolvi | 16,362 | 14,303 | 2,059 | 14 % | 19,355 | 16,491 | 2,864 | 17 % |
| Evkeeza | 3,275 | 212 | 3,063 | * | 7,856 | 365 | 7,491 | * |
| Total product sales | 62,489 | 44,229 | 18,260 | 41 % | 73,805 | 42,179 | 31,626 | 75 % |
| Crysvita royalty revenue | 46,344 | 4,882 | 41,462 | * | 73,221 | 46,331 | 26,890 | 58 % |
| Collaboration and license revenue: | | | | | | | | |
| Crysvita collaboration revenue in Profit-Share Territory | — | 49,906 | (49,906) | * | — | 19,799 | (19,799) | * |
| Daiichi Sankyo | — | 1,479 | (1,479) | * | | | | |
| Total collaboration and license revenue | — | 51,385 | (51,385) | * | — | 19,799 | (19,799) | * |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Total revenues | $ 108,833 | $ 100,496 | $ 8,337 | 8% | $ 147,026 | $ 108,309 | $ 38,717 | 36% |

* Not meaningful

| | Six Months Ended June 30, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Product sales: | | | | |
| Crysvita | $ 76,690 | $ 38,118 | $ 38,572 | 101% |
| Mepsevii | 12,756 | 16,919 | (4,163) | -25% |
| Dojolvi | 35,717 | 30,794 | 4,923 | 16% |
| Evkeeza | 11,131 | 577 | 10,554 | * |
| Total product sales | 136,294 | 86,408 | 49,886 | 58% |
| Crysvita royalty revenue | 119,565 | 51,213 | 68,352 | 133% |
| Collaboration and license revenue: | | | | |
| Crysvita collaboration revenue in Profit-Share Territory | — | 69,705 | (69,705) | * |
| Daiichi Sankyo | — | 1,479 | (1,479) | * |
| Total collaboration and license revenue | — | 71,184 | (71,184) | * |
| Total revenues | $ 255,859 | $ 208,805 | $ 47,054 | 23% |

Our product sales increased by $18.3 million $31.6 million and $49.9 million for the three and six months ended March 31, 2024 June 30, 2024, respectively, compared to the same period periods in 2023. The increase is increases are primarily due to an increase in demand for Crysvita in Latin America resulting from an increase in the number of patients on therapy, launch of Evkeeza in Japan and several markets in Europe, Middle East and Africa territories, or EMEA, and continued increase in demand for our other approved products, and increases in revenue on our named patient programs. products.



Our Crysvita royalty revenue as compared to the and Crysvita collaboration revenue in the Profit-Share Territory increased by a net $7.1 million and decreased by a net $8.4 million $1.4 million for the three and six months ended June 30, 2024, respectively, as compared to the same periods in 2023. The increase for the three months ended March 31, 2024, as compared to June 30, 2024 primarily reflects the same period continuing increase in 2023; this decrease is primarily demand for Crysvita due to recognizing Crysvita royalty revenue in North America on an annual tiered basis for the three months ended March 31, 2024, as compared to the profit-share increase in the prior period. number of patients on therapy. We transitioned commercial responsibilities to KKC in the Profit-Share Territory in April 2023. Post-transition, we recognize our revenue share for Crysvita sales in the Profit-Share Territory as royalty revenue, which was recorded as collaboration revenue prior to the transition. The royalty is calculated using annual revenue tiers ranging from the mid 20% up to 30%. We expect for the year ended 2024, our Crysvita annual tiered royalty revenue for North America will average at the upper end of the range.

Our revenue from the Daiichi Sankyo arrangement decreased by $1.5 million for the three six months ended March 31, 2024 June 30, 2024, compared to the same period periods in 2023. The decrease was due to the completion of the technology transfer and the technology transfer period as of March 31, 2023.

*Cost of Sales (dollars in thousands)*

| | Three Months Ended March 31, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Cost of sales | $ 17,533 | $ 12,257 | $ 5,276 | 43% |

| | Three Months Ended June 30, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Cost of sales | $ 21,280 | $ 9,914 | $ 11,366 | 115% |

| | Six Months Ended June 30, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Cost of sales | $ 38,813 | $ 22,171 | $ 16,642 | 75% |

Cost of sales increased by $5.3 million $11.4 million and $16.6 million for the three and six months ended March 31, 2024 June 30, 2024, respectively, compared to the same period periods in 2023. The increase increases in cost of sales was were due to increased an increase in demand for our approved products. products, primarily Crysvita in

Latin America and Evkeeza in Japan and several markets in EMEA.



*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 business activities: other research and development categories:

| | Three Months Ended March 31, | | Dollar | % | Three Months Ended June 30, | | Dollar | % |
|---|---|---|---|---|---|---|---|---|
| | 2024 | 2023 | Change | Change | 2024 | 2023 | Change | Change |
| Clinical programs: | | | | | | | | |
| Gene therapy programs | $ 52,675 | $ 35,144 | $ 17,531 | 50% | | | | |
| DTX301 | $ 8,386 | $ 7,758 | $ 628 | 8% | | | | |
| DTX401 | 19,770 | 13,710 | 6,060 | 44% | | | | |
| UX701 | 9,385 | 5,340 | 4,045 | 76% | | | | |
| UX111 | 8,406 | 6,016 | 2,390 | 40% | | | | |
| CMC costs | 1,169 | 7,918 | (6,749) | -85% | | | | |
| Total gene therapy programs | 47,116 | 40,742 | 6,374 | 16% | | | | |
| Biologic and nucleic acid programs | 35,887 | 30,854 | 5,033 | 16% | | | | |
| GTX102 | 12,490 | 5,825 | 6,665 | 114% | | | | |
| UX053 | 113 | 3,140 | (3,027) | -96% | | | | |
| UX143 | 19,594 | 13,059 | 6,535 | 50% | | | | |
| Total biologic and nucleic acid programs | 32,197 | 22,024 | 10,173 | 46% | | | | |
| Translational research | 15,690 | 20,424 | (4,734) | -23% | 12,646 | 18,405 | (5,759) | -31% |
| Upfront license, acquisition, and milestone fees | — | 9,000 | (9,000) | * | | | | |
| Approved products | 10,028 | 15,847 | (5,819) | -37% | 6,269 | 14,903 | (8,634) | -58% |
| Infrastructure | 20,882 | 19,538 | 1,344 | 7% | 21,459 | 18,420 | 3,039 | 16% |
| Stock-based compensation | 20,541 | 18,120 | 2,421 | 13% | 21,674 | 19,138 | 2,536 | 13% |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Other research and development | 22,784 | 25,771 | (2,987) | -12% | 20,142 | 22,317 | (2,175) | -10% |
| Total research and development expenses | $ 178,487 | $ 165,698 | $ 12,789 | 8% | $ 161,503 | $ 164,949 | $ (3,446) | -2% |



| | Six Months Ended June 30, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Clinical programs: | | | | |
| Gene therapy programs | | | | |
| DTX301 | $ 23,434 | $ 15,310 | $ 8,124 | 53% |
| DTX401 | 38,109 | 29,320 | 8,789 | 30% |
| UX701 | 21,186 | 11,935 | 9,251 | 78% |
| UX111 | 14,476 | 11,404 | 3,072 | 27% |
| CMC costs | 2,586 | 11,260 | (8,674) | -77% |
| Total gene therapy programs | 99,791 | 79,229 | 20,562 | 26% |
| Biologic and nucleic acid programs | | | | |
| GTX102 | 23,785 | 13,414 | 10,371 | 77% |
| UX053 | 585 | 8,140 | (7,555) | -93% |
| UX143 | 43,714 | 31,324 | 12,390 | 40% |
| Total biologic and nucleic acid programs | 68,084 | 52,878 | 15,206 | 29% |
| Translational research | 28,336 | 38,829 | (10,493) | -27% |
| Upfront license, acquisition, and milestone fees | — | 9,000 | (9,000) | * |
| Approved products | 16,297 | 30,750 | (14,453) | -47% |
| Infrastructure | 42,341 | 37,958 | 4,383 | 12% |
| Stock-based compensation | 42,215 | 37,258 | 4,957 | 13% |
| Other research and development | 42,926 | 44,745 | (1,819) | -4% |
| Total research and development expenses | $ 339,990 | $ 330,647 | $ 9,343 | 3% |

Total research and development expenses decreased by $3.4 million and increased by $12.8 million $9.3 million for the three and six months ended March 31, 2024 June 30, 2024, respectively, compared to the same period periods in 2023. The change in research and development expenses was primarily due to:

- for gene therapy programs, an increase increases of $17.5 million $6.4 million and $20.6 million for the three and six months ended June 30, 2024, respectively, primarily related to continued clinical progress of the DTX301, DTX401, DTX301, UX701 and UX701 UX111 programs and associated internal manufacturing and external manufacturing costs related to the transition of certain programs to in-house manufacturing;
- for biologic and nucleic acid programs, an increase increases of $5.0 million $10.2 million and $15.2 million for the three and six months ended June 30, 2024, respectively primarily related to the continued clinical progress of the UX143 and GTX102 programs and associated clinical development and manufacturing expenses, partially offset a reduction in development expense on UX053 for the treatment of Glycogen Storage Disease Type III; III due to a greater focus on our other late-stage and larger indica clinical programs;
- for translational research, a decrease decreases of $4.7 million $5.8 million and $10.5 million for the three and six months ended June 30, 2024, respectively, primarily related to decreases in manufacturing and headcount expense for IND-stage projects;
- for approved products, upfront license, acquisition, and milestone fees, a decrease of $5.8 million $9.0 million for the three and six months ended June 30, 2024, related fees for achievement of a clinical enrollment milestone for the UX143 program, which was achieved during the three months ended June 30, 2023;
- for approved products, decreases of $8.6 million and $14.5 million for the three and six months ended June 30, 2024, respectively, primarily due to transition of Crysvita commercialization responsibilities in North America to KKC, cost efficiencies on certain disease monitoring program activities, and a decrease in reduced reimbursement Regeneron collaboration expenses associated with pediatric and open label extension trials for Evkeeza;
- for infrastructure, an increase increases of $1.3 million $3.0 million and $4.4 million for the three and six months ended June 30, 2024, respectively, primarily related to increased expenses for support depreciation of our clinical and research program pipeline, expansion of laboratory space, the gene therapy manufacturing facility, depreciation of laboratory-related leasehold improvements and equipment, and IT-related expenses;
- for stock-based compensation, an increase increases of $2.4 million $2.5 million and $5.0 million for the three and six months ended June 30, 2024, respectively, primarily related to higher valuation of stock-based awards granted to employees; and
- for other research and development expenses, a decrease decreases of $3.0 million $2.2 million and $1.8 million for the three and six months ended June 30, 2024, respectively, primarily related to decreased staffing and cost efficiencies to support internal manufacturing, and administrative and general support.

We expect our annual research and development expenses to continue 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 | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Selling, general and administrative | $ 78,160 | $ 76,646 | $ 1,514 | 2% |

| | Three Months Ended June 30, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Selling, general and administrative | $ 80,604 | $ 81,403 | $ (799) | -1% |

| | Six Months Ended June 30, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Selling, general and administrative | $ 158,764 | $ 158,049 | $ 715 | 0% |

Selling, general and administrative expenses decreased by $0.8 million and increased by $1.5 million $0.7 million for the three and six months ended March 31, 2024 June 30, 2024, respectively, compared to the same period periods in 2023. The increase in selling, general and administrative expenses was primarily due to increases in commercialization costs.

We expect annual selling, general and administrative expenses to continue to moderate in the near-term as we continue to support our approved products and multiple clinical-stage product candidates, and thereafter we expect these expenses to increase as we plan to launch additional products.

*Interest Income (dollars in thousands)*

| | Three Months Ended March 31, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Interest income | $ 8,824 | $ 6,290 | $ 2,534 | 40% |

| | Three Months Ended June 30, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Interest income | $ 7,401 | $ 5,964 | $ 1,437 | 24% |

| | Six Months Ended June 30, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Interest income | $ 16,225 | $ 12,254 | $ 3,971 | 32% |

Interest income increased by $2.5 million $1.4 million and $4.0 million for the three and six months ended March 31, 2024 June 30, 2024, respectively, compared to the same period periods in 2023, primarily due to increases in interest rates.

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

| | Three Months Ended March 31, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |

| | | | | |
|---|---|---|---|---|
| Change in fair value of equity investments | $ 3,746 | $ (334) | $ 4,080 | * |

| | Three Months Ended June 30, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Change in fair value of equity investments | $ (3,991) | $ 261 | $ (4,252) | * |

| | Six Months Ended June 30, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Change in fair value of equity investments | $ (245) | $ (73) | $ (172) | 236% |

For the three and six months ended March 31, 2024 June 30, 2024, respectively, we recorded a net increase decreases in the fair value of our equity investments of $3.7 million $4.0 million and $0.2 million due to unrealized gains losses on our investments 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 | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Non-cash interest expense on liabilities for sales of future royalties | $ (15,847) | $ (15,636) | $ (211) | 1% |

| | Three Months Ended June 30, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Non-cash interest expense on liabilities for sales of future royalties | $ (15,960) | $ (15,375) | $ (585) | 4% |



| | Six Months Ended June 30, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Non-cash interest expense on liabilities for sales of future royalties | $ (31,807) | $ (31,011) | $ (796) | 3% |

The non-cash interest expense on liabilities for sales of future royalties decreased increased by a nominal amount $0.6 million and $0.8 million for the three and six months ended March 31, 2024 June 30, 2024, respectively, compared to the same period periods in 2023. 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), Expense (dollars in thousands)*

| | Three Months Ended March 31, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Other income (expense) | $ (1,605) | $ 308 | $ (1,913) | * |

| | Three Months Ended June 30, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Other expense | $ (1,829) | $ (1,989) | $ 160 | -8% |

| | Six Months Ended June 30, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Other expense | $ (3,434) | $ (1,681) | $ (1,753) | 104% |

Other income (expense) expense decreased by $1.9 million $0.2 million and increased by $1.8 million for the three and six months ended March 31, 2024 June 30, 2024, respectively, compared to the same period periods in 2023. These changes were primarily due to fluctuations in foreign exchange rates.

*Provision for Income Taxes (dollars in thousands)*

| | Three Months Ended March 31, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Provision for income taxes | $ (455) | $ (495) | $ 40 | -8% |

| | Three Months Ended June 30, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Provision for income taxes | $ (858) | $ (732) | $ (126) | 17% |

| | Six Months Ended June 30, | | Dollar | % |
|---|---|---|---|---|
| | 2024 | 2023 | Change | Change |
| Provision for income taxes | $ (1,313) | $ (1,227) | $ (86) | 7% |

The provision for incomes taxes decreased increased by a nominal amount for the three and six months ended March 31, 2024 June 30, 2024, respectively, compared to the same period periods in 2023.

**Liquidity and Capital Resources**

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.

As of March 31, 2024 June 30, 2024, we had $568.7 million $874.5 million in available cash, cash equivalents, and marketable debt securities. We believe that our existing capital resources will be sufficient to fund our projected operating requirements for at least the next twelve months. Our cash, cash equivalents, and marketable debt securities are held in a variety of deposit accounts, interest-bearing accounts, corporate bond securities, commercial paper, U.S 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 October 2023, we completed an underwritten public offering in which 9,833,334 shares of common stock were sold, including the exercise in full by the underwriters of their option to purchase an additional 1,500,000 shares, at a public offering price of $30.00 per share. In connection with the offering, we sold to certain investors pre-funded warrants, in lieu of common stock, to purchase 1,666,722 shares of common stock at a purchase price of $29.999 per pre-funded warrant, which equals the public offering price per share of common stock less the $0.001 exercise price per share of each pre-funded warrant. The total proceeds that we received from the offering were $326.5 million, net of underwriting discounts and commissions.

In June 2024, we completed an underwritten public offering in which 8,782,051 shares of common stock were sold, including the exercise in full by the underwriters of their option to purchase an additional 1,346,153 shares, at a public offering price of $39.00 per share. In connection with the offering, we sold to certain investors pre-funded warrants, in lieu of common stock, to purchase 1,538,501 shares of common stock at a purchase price of $38.999 per pre-funded warrant, which equals the public offering price per share of common stock less the $0.001 exercise price per share of each pre-funded warrant. The total proceeds that we received from the offering were $380.9 million, net of underwriting discounts and commissions.



As of March 31, 2024 June 30, 2024, none of the pre-funded warrants had been exercised.

In February 2024, we entered into a Sales Agreement with Cowen and Company, LLC, or Cowen, pursuant to which the Company may offer and sell shares of the Company's common stock having an aggregate offering proceeds up to $350.0 million, from time to time, in ATM offerings through Cowen. No shares were sold under this agreement during the three six months ended March 31, 2024 June 30, 2024.

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

| | Three Months Ended March 31, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2024 | 2023 | 2024 | 2023 |
| Cash used in operating activities | $ (190,727) | $ (156,867) | $ (267,690) | $ (273,028) |
| Cash provided by investing activities | 94,435 | 111,304 | 154,999 | 210,722 |
| Cash used in financing activities | (58) | (722) | | |
| Cash provided by financing activities | 384,881 | 32,298 | | |
| Effect of exchange rate changes on cash | (679) | 211 | (1,327) | 75 |
| Net decrease in cash, cash equivalents and restricted cash | $ (97,029) | $ (46,074) | | |
| Net increase (decrease) in cash, cash equivalents and restricted cash | $ 270,863 | $ (29,933) | | |

***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 six months ended March 31, 2024 June 30, 2024 was $190.7 million $267.7 million and primarily reflected a net loss of $170.7 million $302.3 million, partially offset by non-cash items of $36.0 million $74.3 million, net, which consisted primarily of stock-based compensation, amortization of discounts on marketable debt securities, depreciation and amortization, change in fair value of equity investments, non-cash collaboration royalty revenues, revenue, and non-cash interest expense related to the sale of future royalties to RPI Finance Trust, or RPI, an affiliate of Royalty Pharma, and OMERS, stock-based compensation, amortization of discounts on marketable debt securities, the change in fair value of equity investments, and depreciation and amortization. to OCM LS23 Holdings LP, an investment vehicle for Ontario Municipal Employees Retirement System, or OMERS. The change in operating assets and liabilities also reflected a net use of cash of $56.0 million $39.7 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 combined with a net decrease in accounts payable, accrued and other liabilities primarily due to the payout of the 2023 annual bonus and decreases in accrued collaboration for the payment of a regulatory milestone to Regeneron. Medicaid obligations.

Cash used in operating activities for the three six months ended March 31, 2023 June 30, 2023 was $156.9 million $273.0 million and primarily reflected a net loss of $164.0 million $323.8 million, partially offset by non-cash items of $45.5 million $82.0 million, net, which consisted primarily of non-cash collaboration



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royalty revenues, interest expense related to the sale of future royalties to RPI and OMERS, net of amounts capitalized, stock-based compensation, amortization of discounts on marketable debt securities, and depreciation and amortization. The change in operating assets and liabilities also reflected a net use of cash of $38.4 million $31.2 million, primarily due to a net decrease in accounts payable, accrued liabilities, and other liabilities, primarily due to timing of payments and receipt of invoices, as well as a decrease in manufacturing accruals and general corporate accruals, and the payout of the 2022 annual bonus and decreases bonuses, combined with an increase in manufacturing accruals accounts receivable, primarily related to an increase in sales of our approved products and timing of invoicing. when orders were received, partially offset a net decrease in prepaid expenses and other assets primarily related to a decrease in prepaid manufacturing.

***Cash Provided by Investing Activities***

Cash provided by investing activities for the three six months ended March 31, 2024 June 30, 2024 was $94.4 million $155.0 million and was primarily related to $109.7 million $174.8 million from net activities in marketable debt securities, offset by the payment payments to Regeneron of $10.0 million $12.5 million for the achievement of a milestone milestones under the collaboration agreement recorded as an intangible asset.

Cash provided by investing activities for the three six months ended March 31, 2023 June 30, 2023 was $111.3 million $210.7 million and was primarily related to $140.3 million $256.5 million from net activities in marketable debt securities, offset by purchases of property, plant, and equipment of $25.0 million $39.0 million, primarily related to the fit-out of our gene therapy manufacturing facility.

***Cash used in Provided by Financing Activities***

Cash used in provided by financing activities for the three six months ended March 31, 2024 June 30, 2024 was $0.1 million. $384.9 million and was primarily related to proceeds from issuance of common stock and pre-funded warrants in connection with the underwritten public offering, net.

Cash used in provided by financing activities for the three six months ended March 31, 2023 June 30, 2023 was $0.7 million. $32.3 million, primarily related to proceeds from our ATM offering, net.

**Funding Requirements**

We anticipate that, excluding non-recurring items, we will continue to generate annual losses for the foreseeable future next several years 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 the general economic slowdown, inflationary pressure, high interest rates, and potential recessionary environment or 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, 2024 June 30, 2024, were approximately $51.1 million $46.8 million, of which $16.2 million $14.9 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, 2024 June 30, 2024, we had obligations of approximately $32.7 million $40.4 million, of which $23.5 million $23.6 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, 2024 June 30, 2024, we had cash, cash equivalents, and marketable debt securities totaling $568.7 million $874.5 million, compared to $777.1 million as of December 31, 2023, 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, 2024 June 30, 2024 or December 31, 2023. To date, we have not experienced a loss of principal on any of our investments and as of March 31, 2024 June 30, 2024, we did not record any allowance for credit loss from our investments.

**Foreign Currency Risk**

We face foreign exchange risk as a result of entering into transactions denominated in currencies other than U.S. dollars. Due to the uncertain timing of expected payments in foreign currencies, we do not utilize any forward exchange contracts. All foreign transactions settle on the applicable spot exchange basis at the time such payments are made. Volatile market conditions arising from the 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 and six months ended March 31, 2024 June 30, 2024, a majority of our revenue, expenses, and capital expenditures were denominated in U.S. dollars. A hypothetical 10% change in foreign exchange rates during any of the periods presented would not have had a material impact on our Condensed Consolidated Financial Statements.



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***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, 2024 June 30, 2024. For the purpose of this review, disclosure controls and procedures means controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit is recorded, processed, summarized and reported within the time periods specified in the SEC’s rules and forms. These disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit is accumulated and communicated to management, including our Principal Executive Officer and 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, 2024 June 30, 2024, that has materially affected, or is reasonably likely to materially affect our internal control over financial reporting.



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**PART II. OTHER INFORMATION**

**Item 1. *Legal Proceedings***

We are not currently a party to any material legal proceedings. We may, however, in the ordinary course of business face various claims brought by third parties or government regulators and we may, from time to time, make claims or take legal actions to assert our rights, including claims relating to our directors, officers, stockholders, intellectual property rights, employment matters and the safety or efficacy of our products. Any of these claims could subject us to costly litigation and, while we generally believe that we have adequate insurance to cover many different types of liabilities, our insurance carriers may deny coverage, may be inadequately capitalized to pay on valid claims, or

our policy limits may be inadequate to fully satisfy any damage awards or settlements. If this were to happen, the payment of any such awards could have a material adverse effect on our consolidated operations, cash flows and financial position. Additionally, any such claims, whether or not successful, could damage our reputation and business.

**Item 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. 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 anticipate that we will continue to incur losses for the foreseeable future.
- 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 m lead to faster development or approval.
- Our product candidates may cause undesirable or serious side effects.
- We face a multitude of manufacturing risks, particularly with respect to our gene therapy and mRNA product candidates.
- Our products remain subject to regulatory scrutiny even if we obtain regulatory approval.
- Product liability lawsuits against us could cause us to incur substantial liabilities.



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- We may not realize the full commercial potential of our product candidates if we are unable to source and develop effective biomarkers.
- We rely on third parties to conduct our nonclinical and clinical studies and perform other tasks for us.
- We are dependent on KKC for the clinical and commercial supply of Crysvita for all major markets and for the development and commercialization of Crysvita in certai major markets.
- We rely on third parties to manufacture our products and product candidates.
- The loss of, or failure to supply by, any of any of our single-source suppliers for our drug substance and drug product could adversely affect our business.
- The actions of distributors and specialty pharmacies could affect our ability to sell or market products profitably.
- Our revenue may be adversely affected if the market opportunities for our products and product candidates are smaller than expected.
- Our competitors may develop therapies that are similar, more advanced, or more effective than ours.
- We may not successfully manage expansion of our company, including building an integrated commercial organization.
- After the transition of our commercialization responsibilities for Crysvita in the U.S. and Canada, the success of Crysvita in those territories is dependent on the effectiveness of KKC's commercialization efforts.
- Commercial success of our products depends on the degree of market acceptance.

- We face uncertainty related to insurance coverage and reimbursement status of our newly approved products.
- If we, or our third-party partners, are unable to maintain effective proprietary rights for our products or product candidates, we may not be able to compete effectively.
- Claims of intellectual property infringement may prevent or delay our development and commercialization efforts.
- We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.
- We may face competition from biosimilars of our biologics product and product candidates or from generic versions of our small-molecule product and product candida 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 a 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 owners 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 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.



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- 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 a 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 employ
- 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 our net operating loss carryforwards, costs of litigation, stockholder activism and increased scrutiny regarding our ESG practices and disclosures.

**Risks Related to Our Financial Condition and Capital Requirements**

***We have a history of operating losses and anticipate that we will continue to incur losses for the foreseeable future.***

We are a biopharmaceutical company with a history of operating losses, and anticipate continuing to incur operating losses for the foreseeable future. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We have devoted substantially all of our financial resources to identifying, acquiring, and developing our products and product candidates, including conducting clinical studies, developing manufacturing processes, manufacturing product candidates for clinical studies, and providing selling, general and administrative support for these operations. The amount of our future net losses will depend, in part, on non-recurring events, the success of our commercialization efforts, and the rate of our future expenditures. We anticipate that our expenses will increase substantially if and as we:

- continue our research and nonclinical and clinical development of our product candidates;
- expand the scope of our current clinical studies for our product candidates;
- advance our programs into more expensive clinical studies;
- initiate additional nonclinical, clinical, or other studies for our product candidates;
- pursue preclinical and clinical development for additional indications for existing products and product candidates;
- change or add additional manufacturers or suppliers;
- expand upon our manufacturing-related facilities and capabilities, particularly as we continue to ramp-up 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 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; a
- 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 o regulatory challenges that require longer follow-up of existing studies, additional major studies, or additional supportive studies in order to pursue marketing approval.



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The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

***We have limited experience in generating revenue from product sales.***

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

- obtaining regulatory and marketing approvals with broad indications for product candidates for which we complete clinical studies;
- developing a sustainable and scalable manufacturing process for our products and any approved product candidates and establishing and maintaining supply and manufacturing relationships with third parties that can conduct the processes and provide adequate (in amount and quality) product supply to support market demand fo 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 s
- 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, 2024 June 30, 2024, our available cash, cash equivalents, and marketable debt securities were $568.7 million $874.5 million. We expect we will may need additional capital to continue to commercialize our products, and to develop and obtain regulatory approval for, and to commercialize, all of our product candidates. In addition, our operating plans may change as a result of many factors that may currently be unknown to us, and we may need to seek additional funds sooner than planned. Our future funding requirements will depend on many factors, including but not limited to:

- the scope, rate of progress, results, and cost of our clinical studies, nonclinical testing, and other related activities;
- the cost of manufacturing clinical and commercial supplies of our products and product candidates;
- the cost of creating additional infrastructure, including facilities and systems, such as 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;



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- the cost and timing of establishing and operating our international subsidiaries;
- the cost and timing of establishing and operating field forces, marketing, and distribution capabilities;
- the cost and timing of other activities needed to commercialize our products; and
- the terms and timing of any collaborative, licensing, acquisition, and other arrangements that we may establish, including any required milestone, royalty, and reimbursements or other payments thereunder.

Any additional fundraising efforts may divert our management's attention from their day-to-day activities, which can adversely affect our ability to develop our product candidates and commercialize our products. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all, particularly in light of the current macroeconomic conditions, including the general economic slowdown and potential recessionary environment. The terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities by us, whether equity or debt, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. If we incur debt, it could result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell, or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. We have in the past sought and may in the future seek funds through a sale of future royalty payments similar to our transactions with Royalty Pharma and OMERS or through collaborative partnerships, strategic alliances, and licensing or other arrangements, such as our transaction with Daiichi Sankyo 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 may not be able to access a portion of our existing cash, cash equivalents and investments due to market conditions. If banks or financial institutions enter receivership or become insolvent in the future, similar to what occurred at Silicon Valley Bank in March 2023, or if there is a concern that they may do so in response to financial conditions affecting the banking system and financial markets, our ability to access our existing cash, cash equivalents and investments may be threatened and the value of our investments may be significantly impaired.

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, messenger RNA, or mRNA, DNA, small interfering RNA, or siRNA, or other novel and complex product candidates, which 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 o 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 clinica 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 inabilit 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.



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***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. Applications for our product candidates could fail to receive regulatory approval, or could be delayed in receiving regulatory approval, for many reasons, including but not limited to the following:

- regulatory authorities may disagree with the design, implementation, or conduct of our clinical studies;
- regulatory authorities may change their guidance or requirements for a development program for a product candidate;
- the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approv
- 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 c submission or to obtain regulatory approval;



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- we may be unable to demonstrate to regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities used to manufacture our clinical and commercial supplies;
- the U.S. government may be shut down, which could delay the FDA;
- the FDA may be delayed in responding to our applications or submissions due to competing priorities or limited resources, including as a result of the lack of FDA fundin personnel;
- failure of our nonclinical or clinical development to comply with an agreed upon Pediatric Investigational Plan, or PIP, which details the designs and completion timelines 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" or 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 current PRV Voucher Program is scheduled to sunset such that the FDA may only award a PRV for a product application if a company receives the rare pediatric disease designation from the FDA for the product candidate by September 30, 2024, and the FDA will cease awarding PRVs after September 30, 2026. Extension of the current PRV Voucher Program is subject to approval by Congress and it is currently uncertain whether the program will be extended. If our qualifying product candidates are approved by the FDA after the current approval deadlines, we will not be eligible to receive additional PRVs for our product candidates and accordingly, we would be unable to use such PRV for Priority Review for another one of our programs or to sell such PRV, which sale has the potential to generate significant proceeds.



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

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

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

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

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

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

Gene therapy remains a novel technology. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. For example, certain gene therapy trials using AAV8 vectors (although at significantly higher doses than those used in our gene therapy product candidates) and other vectors led to several well-publicized adverse events, including cases of leukemia and death. The risk of cancer or death remains a concern for gene therapy and we cannot assure you that it will not occur in any of our planned or future clinical studies. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. Serious adverse events in our clinical trials, or other clinical trials involving gene therapy products, particularly AAV gene therapy products such as candidates based on the same capsid serotypes as our product candidates, or occurring during use of our competitors' products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity, could result in increased government regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our gene therapy product candidates, stricter labeling requirements for those gene therapy product candidates that are approved and a decrease in demand for any such gene therapy product candidates.

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

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

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

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

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

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



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

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

***We are dependent on KKC for the clinical and commercial supply of Crysvita for all major markets and for the development and commercialization of Crysvita in certain major markets, and KKC's failure to provide an adequate supply of Crysvita or to commercialize Crysvita in those markets could result in a material adverse effect on our business and operating results.***

Under our agreement with KKC, KKC has the sole right to commercialize Crysvita in Europe and, at certain specified times, in the U.S., Canada, and Turkey, subject to certain rights retained. Our partnership with KKC may not be successful, and we may not realize the expected benefits from such partnership, due to a number of important factors,

including but not limited to the following:

- KKC has no obligation under our agreement to use diligent efforts to commercialize Crysvita in Europe, the U.S., or Canada. The timing and amount of any royalty payments that are made by KKC based on sales of Crysvita in Europe, the U.S., and Canada will depend on, among other things, the efforts, allocation of resources, an successful commercialization of Crysvita by KKC in those territories;
- 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 imp 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 clinic 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 Crys 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 n 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 grea than anticipated.

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

As we currently lack the resources and the full capability to manufacture all of our products and product candidates on a clinical or commercial scale, we rely on third parties to manufacture our products and product candidates. Although we oversee the contract manufacturers, we cannot control the manufacturing process of, and are substantially dependent on, our contract manufacturing partners for compliance with the regulatory requirements. See "- *Even if we obtain regulatory approval for our product candidates, our products remain subject to regulatory scrutiny"* risk factor above. Further, we depend on our manufacturers to purchase from third-party suppliers the materials necessary to produce our products and product candidates. There are a limited number of suppliers for raw materials that we use to manufacture our drugs, placebos, or active controls, and there may be a need



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to identify alternate suppliers to prevent or mitigate a possible disruption of the manufacture of the materials necessary to produce our products and product candidates for our clinical studies, and, if approved, ultimately for commercial sale. We also do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. We may also experience interruptions in supply of product if the product or raw material components fail to meet our quality control standards or the quality control standards of our suppliers.

Further, manufacturers that produce our products and product candidates may not have experience producing our products and product candidates at commercial levels and may not produce our products and product candidates at the cost, quality, quantities, locations, and timing needed to support profitable commercialization. We have not yet secured manufacturing capabilities for commercial quantities of all of our product candidates and may be unable to negotiate binding agreements with manufacturers to support our commercialization activities on commercially reasonable terms. Even if our third-party product manufacturers develop acceptable manufacturing processes that provide the necessary quantities of our products and product candidates in a compliant and timely manner, the cost to us for the supply of our products and product candidates manufactured by such third parties may be high and could limit our profitability. For instance, KKC is our sole supplier of commercial quantities of Crysvita. The supply price to us for commercial sales of Crysvita in Latin America and the transfer price for commercial sales of the product in the U.S. and Canada was 35% of net sales through December 31, 2022 and 30% thereafter, which is higher than the typical cost of sales for companies focused on rare diseases.

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

- The process of manufacturing our products and product candidates is extremely susceptible to product loss due to contamination, equipment failure or improper installat 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 Regeneron pursuant to a supply agreement. The drug substance and drug product for Mepsevii are currently manufactured by Rentschler under a commercial supply and services agreement, accompanying purchase orders, and other agreements. Pharmaceutical-grade drug substance for Dojolvi is manufactured by IOI Oleo pursuant to a supply agreement, and the drug product for Dojolvi was prepared by Haupt Pharma AG, pursuant to a master services agreement. Single source suppliers are also used for our gene therapy programs. Haupt Pharma closed its Wolfrathshausen, Germany site, which produces the Dojolvi drug product, at the end of 2023. As such, we are in the process of qualifying and conducting transfer activities to an alternative supplier. We cannot provide assurances that qualifying alternate sources, if available at all, for the Dojolvi drug product or for any of our other 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, current geopolitical tensions with China including the Congressional legislative proposal, titled the BIOSECURE Act, which would, among other things, prohibit U.S. federal funding in connection with biotechnology equipment or services produced or provided by Chinese biotechnology companies, and the recent requests by certain Congressional leaders that WuXi AppTech Co. and its affiliates be added to certain U.S. Government restricted entity lists, could lead to our competitors and other companies moving to suppliers outside of China, including to our current suppliers. Significant increases in business at our single source suppliers resulting from such activities could adversely limit capacity at such suppliers to manufacture our products or result in price increases, interruptions or delays of our products.

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

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



**Risks Related to Commercialization of Our Products and Product Candidates**

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

We focus our research and product development on treatments for rare and ultrarare genetic diseases. Given the small number of patients who have the diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare and ultrarare genetic diseases. Some of our current products or clinical programs may also be most appropriate for patients with more severe forms of their disease. For instance, while adults make up the majority of the XLH patients, they often have less severe disease that may reduce the penetration of Crysvita in the adult population relative to the pediatric population. Given the overall rarity of the diseases we target, it is difficult to project the prevalence of the more severe forms, or the other subsets of patients that may be most suitable to address with our products and

product candidates, which may further limit the addressable patient population to a small subset. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our products and product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations, or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for each of our products and product candidates may be limited or may not be amenable to treatment with our products and product candidates, and new patients may become increasingly difficult to identify or access. Further, even if we obtain significant market share for our products and product candidates, because the potential target populations are very small, we may never become or remain profitable nor generate sufficient revenue growth to sustain our business.

***We face intense competition and rapid technological change 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 our “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.

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

We expect to need additional managerial, operational, marketing, financial, legal, and other resources to support our development and commercialization plans and strategies. In order to successfully commercialize our products as well as any additional products that may result from our development programs or that we acquire or license from third parties, we are expanding our commercial infrastructure 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 will be expanded as we approach the potential approval dates of additional products that result from our development programs. Our management may need to divert a disproportionate amount of



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

We, as a company, have limited, recent experience selling and marketing our product and only some of our employees have prior experience promoting other similar products while employed at other companies. As we increase the number and range of our commercialized products, we may experience additional complexities in our sales process and strategy and may encounter difficulties in allocating sufficient resources to sales and marketing of certain products. Further, as we launch additional products or as demand for our products change, our initial estimate of the size of the required field force may be materially more or less than the size of the field force actually required to effectively commercialize our product candidates. As such, we may be required to hire larger teams to adequately support the commercialization of our products and product candidates or we may incur excess costs in an effort to optimize the hiring of commercial personnel. With respect to certain geographical markets, we may enter into collaborations with other entities to utilize their local marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If our future collaborators do not commit sufficient resources to commercialize our future products, if any, and we are unable to develop the necessary marketing capabilities on our own, we will be unable to generate sufficient product 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.

***Our exclusive rights to promote Crysvita in the U.S. and Canada transitioned back to KKC and the success of Crysvita in those territories are dependent on the effectiveness of KKC's commercialization efforts.***

Pursuant to the terms of our collaboration and license agreement with KKC, or the collaboration agreement, we had the sole right to promote Crysvita in the U.S. and Canada, or the Profit-Share Territory, for a specified period of time, with KKC increasingly participating in the promotion of the product until the transition date of April 2023. At the transition date, commercialization responsibilities for Crysvita in the Profit-Share Territory transitioned to KKC, and KKC assumed responsibility for the commercialization of the product in the territory. After the transition date, the commercial success of Crysvita in the Profit-Share Territory depends on, among other things, the efforts and allocation of resources of KKC, which we do not control. Failure by KKC to successfully market and sell Crysvita in the United States could have an adverse effect on our financial results.

***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.



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

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

Our target patient populations are small, and accordingly the pricing, coverage, and reimbursement of our products and product candidates, if approved, must be adequate to support our commercial infrastructure. Our per-patient prices must be sufficient to recover our development and manufacturing costs and potentially achieve profitability. We expect the cost of a single administration of gene therapy products, such as those we are developing, to be substantial, when and if they achieve regulatory approval. Accordingly, the availability and adequacy of coverage and reimbursement by governmental and private payors are essential for most patients to afford expensive treatments such as ours, assuming approval. Sales of our products and product candidates, if approved, will depend substantially, both domestically and abroad, on the extent to which their costs will be paid for by health maintenance, managed care, pharmacy benefit, and similar healthcare management organizations, or reimbursed by government authorities, private health insurers, and other payors. If coverage and reimbursement are not available, are available only to limited levels, or are not available on a timely basis, we may not be able to successfully commercialize our products and product candidates, if approved. For example, deteriorating economic conditions and political instability in certain Latin American countries and in Turkey continue to cause us to experience significant delays in receiving approval for reimbursement for our products and consequently impact our product commercialization timelines in such regions. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to sustain our overall enterprise. In addition, we do not know the reimbursement rates until we are ready to market the product and we actually negotiate the rates.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the U.S., the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, decides whether and to what extent a new drug will be covered and reimbursed under

Medicare. Private payors tend to follow the coverage reimbursement policies established by CMS to a substantial degree. It is difficult to predict what CMS or private payors will decide with respect to reimbursement for products such as ours, especially our gene therapy product candidates as there is a limited body of established practices and precedents for gene therapy products.

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



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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, patents will issue, the breadth of any such patent, or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful opposition to these patents could impair the exclusivity position of our products or deprive us of rights necessary for the successful commercialization of any product candidates that are approved. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

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

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

Patents have a limited lifespan. In the U.S., the natural expiration of a patent is generally 20 years 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.



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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 invention claimed in our owned and in-licensed patents or pending applications, or that we or our licensor were the first to file for patent protection of such inventions.

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

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 is relevant or necessary to the commercialization of our products or product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that are relevant to our products or product candidates.

We are aware of certain U.S. and foreign patents owned by third parties that a court might construe to be valid and relevant to one or more of our gene therapy product candidates, certain methods that may be used in their manufacture or delivery, or certain formulations comprising one or more of our gene therapy candidates. Regarding our anti-sclerostin antibody product candidate, setrusumab, we are aware of litigation involving patents owned by a third-party, OssiFi-Mab LLC, orOMab, 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.



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

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

Accordingly, competitors could file ANDAs for generic versions of our small-molecule product, Dojolvi, or 505(b)(2) NDAs that reference Dojolvi. For the patents listed for Dojolvi in the Orange Book, those ANDAs and 505(b)(2) NDAs would be required to include a certification as to each listed patent indicating whether the ANDA applicant does or does not intend to challenge the patent. We cannot predict how any generic competitor would address such patents, whether we would sue on any such patents, or the outcome of any such suit.

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 have received requests for samples of Dojolvi, and when appropriate, we have sold samples of Dojolvi to eligible product developers in compliance with the requirements of the CREATES Act.

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 competitors develop generic version of Dojolvi and are able to enter the market, 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.

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

Competitors may infringe our patents or the patents of our licensors. If we or one of our licensing partners were to initiate legal proceedings against a third party to enforce a patent covering our products or one of our product candidates, the defendant could counterclaim that the patent covering our product or product candidate is invalid and/or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable.

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



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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. For example, with respect to patent term adjustment, or PTA, the Federal Circuit's recent holding in In re *Cellect, LLC*, 81 F.4th 1216 (Fed. Cir. 2023), that the obviousness-type double patenting analysis for a patent that has received PTA must be based on the expiration date of the patent after the PTA has been added, may negatively impact the validity and/or term of certain of our owned or in-licensed U.S. patents.

***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.***

We completed construction of our gene therapy manufacturing facility in Bedford, Massachusetts in 2023. Prior to construction of this facility, 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, particularly as we have only recently commenced our manufacturing operations. Our limited experience 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. Over the last several years, we have also experienced certain executive leadership changes. Leadership transitions are inherently difficult to manage, cause uncertainty and disruption and could increase the likelihood of turnover of other key officers and employees. The inability to recruit and retain qualified personnel, or the loss of the services of Dr. Kakkis or any of other member of our executive leadership team or other key employee, may impede the progress of our research, development, and commercialization objectives.

***If we fail to obtain or maintain orphan drug exclusivity for our products, our competitors may sell products to treat the same conditions and our revenue will be reduced.***

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

Because the extent and scope of patent protection for our products may in some cases be limited, orphan drug designation is especially important for our products for which orphan drug designation may be available. For eligible drugs, we plan to rely on the exclusivity period under the Orphan Drug Act to maintain a competitive position. If we do not obtain orphan drug exclusivity for our drug products and biologic products that do not have broad patent protection, our competitors may then sell the same drug to treat the same condition sooner than if we had obtained orphan drug exclusivity, and our revenue will be reduced.

Even though we have orphan drug designation for 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 an intangible asset related to our license from Regeneron for Evkeeza. We test the intangible assets for impairment annually during the fourth quarter and more frequently if events or changes in circumstances indicate that it is more likely than not that the asset is impaired. If the associated research and development effort is abandoned, the related assets will be written-off and we will record a noncash impairment loss on our Condensed Consolidated Statement of Operations. We have not recorded any impairments related to our intangible assets through March 31, 2024 June 30, 2024.

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

The success of our business depends upon our ability to identify, license, discover, develop, or commercialize additional product candidates in addition to the continued clinical testing, potential approval, and commercialization of our existing product candidates. Research programs to identify and develop new product candidates require substantial technical, financial, and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. Our research programs or licensing efforts may fail to yield additional product candidates for clinical development and commercialization for a number of reasons, including but not limited to the following:

- our research or business development methodology or search criteria and process may be unsuccessful in identifying potential product candidates;
- we may not be able or willing to assemble sufficient technical, financial or human resources to acquire or discover additional product candidates;
- we may face competition in obtaining and/or developing additional product candidates;
- our product candidates may not succeed in research, discovery, preclinical or clinical testing;
- our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval;



- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop may be covered by third parties' patents or other exclusive rights;
- the market for a product candidate may change during our program so that such a product may become unreasonable to continue to develop;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost or at all; and

- a product candidate may not be accepted as safe and effective by regulatory authorities, patients, the medical community, or payors.

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

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

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

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

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

In particular, our operations are directly, and indirectly through our customers, subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and physician sunshine laws and regulations; and patient and non-patient privacy regulations, including the GDPR and the California Consumer Privacy Act, or CCPA, including amendments from the California Privacy Rights Act, or CPRA, as described 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.



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

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment,

disgorgement of profits, and the curtailment or restructuring of our operations. If any governmental sanctions, fines, or penalties are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, operating results, financial condition and our reputation could be harmed. In addition, responding to any action will likely result in a significant diversion of management's attention and resources and an increase in professional fees.

Our research and development activities, including our process and analytical development activities in our quality control laboratory, and our and our third-party manufacturers' and suppliers' activities, 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. Doing business internationally involves a number of risks, including but not limited to:



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- multiple, conflicting, and changing laws and regulations such as privacy and data regulations, transparency regulations, tax laws, export and import restrictions, employr laws, regulatory requirements, and other governmental approvals, permits, and licenses;
- introduction of new health authority requirements and/or changes in health authority expectations;
- failure by us to obtain and maintain regulatory approvals for the use of our products in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection for, and enforcing, our intellectual property;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;
- limits on our ability to penetrate international markets;
- financial risks, such as longer payment cycles, additional or more burdensome regulatory requirements of financial institutions outside of the U.S., difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products, and exposure to foreign currency exchange rate fluctuati
- 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, rising inflation, the potential recessionary environment, the potential shutdown of the U.S. federal government, boycotts an 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 tl 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 foreig 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 business and operations may be materially adversely affected in the event of computer system failures or security breaches.***

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

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

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



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- 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, rising inflation, and the potential recessionary environment;
- sales of our common stock by us or our stockholders in the future; and
- trading volume of our common stock.

In addition, biotechnology and biopharmaceutical companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

***Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.***

We will need additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities, or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities, or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

In June 2023, we adopted our 2023 Incentive Plan, or the 2023 Plan, which replaced our 2014 Incentive Plan and was amended and restated in June 2024, following stockholder approval of the plan. Pursuant to our 2023 Plan, our management is authorized to grant stock options and other equity-based awards to our employees, directors, and consultants. At March 31, 2024 June 30, 2024, there were 1,398,838 1,711,846 shares available for future grants under the 2023 Plan.

Pursuant to our 2014 Employee Stock Purchase Plan, which was amended and restated in June 2023, 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, 2024 June 30, 2024, there were 6,694,377 6,567,545 shares available for issuance under the A&R ESPP.

Our board of directors has adopted an Employment Inducement Plan, which was amended in June 2023, or the Inducement Plan, with a maximum of 850,000 shares available for grant under the plan. At March 31, 2024 June 30, 2024, there were 115,324 23,673 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 person 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;



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- 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 resta 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.



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

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

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

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

***Litigation may substantially increase our costs and harm our business.***

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

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

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



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

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

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

**Item 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, 2024 June 30, 2024, 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 |
|---|---|---|---|
| Emil Kakkis Dennis Huang<br>EVP, Chief Executive Technical Operations Officer, and Director Gene Therapy Research & Development | March 1, May 7, 2024 | Up to 85,000 shares | February 28, 2025 |
| Karah Parschauer<br>EVP, Chief Legal Officer and Corporate Affairs | March 5, 2024 | Up to 41,717 shares, 31,911 of which are shares to be acquired upon the exercise of stock options | March 5, 2025 |
| Shehnaaz Suliman,<br>Board Member | March 8, 2024 | Up to 25,000 75,000 shares, all of which are shares to be acquired upon the exercise of stock options | March 7, July 15, 2025 |

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|---|---|---|---|
| Eric Crombez John Pinion<br>Chief Quality Operations Officer and EVP, Chief Medical Officer Translational Sciences | March 11, May 7, 2024 | Up to 61,247 109,730 shares, 37,266 107,800 of which are shares to be acquired upon the exercise of stock options | March 14, May 7, 2025 |



**Item 6. *Exhibits***

| | | Incorporated by Reference | | | Furnished or Filed |
|---|---|---|---|---|---|
| **Exhibit Number** | **Exhibit Description** | **Form** | **Date** | **Number** | **Herewith** |
| 3.1 | Amended and Restated Certificate of Incorporation | 8-K | 2/5/2014 | 3.1 | |
| 3.2 | Amended and Restated Bylaws | 8-K | 2/5/2014 | 3.2 | |
| 4.1 | Form of Common Stock Certificate | S-1 | 11/8/2013 | 4.2 | |
| 4.2 | Form of Indenture | S-3ASR | 2/21/2024 | 4.2 | |
| 4.3 | Form of Pre-Funded Warrant | 8-K | 10/23/2023 | 4.1 | |
| 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). | | | | |

| | | Incorporated by Reference | | | Furnished or Filed |
|---|---|---|---|---|---|
| **Exhibit Number** | **Exhibit Description** | **Form** | **Date** | **Number** | **Herewith** |
| 3.1 | Amended and Restated Certificate of Incorporation | 8-K | 2/5/2014 | 3.1 | |
| 3.2 | Amended and Restated Bylaws | 8-K | 2/5/2014 | 3.2 | |
| 4.1 | Form of Common Stock Certificate | S-1 | 11/8/2013 | 4.2 | |
| 4.2 | Form of Indenture | S-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# | Amended and Restated 2023 Incentive Plan | S-8 | 7/12/2024 | 4.4 | |
| 10.2# | Second Amendment to Employment Inducement Plan | S-8 | 7/12/2024 | 4.7 | |
| 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). | |

* 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.

# Indicates management contract or compensatory plan



**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 2, 2024 August 1, 2024

By: /s/ Emil D. Kakkis

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

President and Chief Executive Officer and Director

(Principal Executive Officer)

Date: May 2, 2024 August 1, 2024

By: /s/ Howard Horn

Howard Horn

Executive Vice President, Chief Financial Officer, Corporate Strategy

(Principal Financial Officer)

Date: May 2, 2024 August 1, 2024

By: /s/ Theodore A. Huizenga

Theodore A. Huizenga

Senior Vice President and Chief Accounting Officer

(Principal Accounting Officer)

**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 o 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) 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 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 reasor assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accou 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 disclosur 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 registr 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 financia 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 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 affec 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 2, 2024 August 1, 2024

/s/ Emil D Kakkis

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

President and Chief Executive Officer

(Principal Executive Officer)

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**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 o 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) 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

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 reasor assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accou 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 disclosur 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 registr 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 financia 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 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 affec 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 2, 2024 August 1, 2024

/s/ Howard Horn

Howard Horn

Executive Vice President, Chief Financial Officer, Corporate Strategy

(Principal Financial Officer)

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**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, 2024 June 30, 2024 (the "Report"), I, Emil D. Kakkis, M.D., Ph.D., as President and Chief Executive Officer of the Company, and Howard Horn, as Executive Vice President 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 2, 2024 August 1, 2024

/s/ Emil D. Kakkis

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

President and Chief Executive Officer

(Principal Executive Officer)

Dated: May 2, 2024 August 1, 2024

/s/ Howard Horn

Howard Horn

Executive Vice President, Chief Financial Officer, Corporate Strategy

(Principal Financial Officer)

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