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# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**Washington, D.C. 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, 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 number: 001-36167**

# Karyopharm Therapeutics Inc.
**(Exact name of registrant as specified in its charter)**

| **Delaware** | **26-3931704** |
|---|---|
| **(State or other jurisdiction of incorporation or organization)** | **(I.R.S. Employer Identification Number)** |
| **85 Wells Avenue, 2nd Floor** | |
| **Newton , MA** | **02459** |
| **(Address of principal executive offices)** | **(Zip Code)** |

**( 617 ) 658-0600**
**(Registrant's telephone number, including area code)**

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

| **Title of each class** | **Trading Symbol(s)** | **Name of each exchange on which registered** |
|---|---|---|
| Common Stock , $0.0001 par value | KPTI | Nasdaq Global Select Market |

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

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

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

| | |
|---|---|
| Large accelerated filer ☐ | Accelerated filer ☒ |

Non-accelerated filer ☐ Smaller reporting company ☐

Emerging growth company ☐

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

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

As of May 3, 2024, there were

117,710,263
shares of Common Stock, $0.0001 par value per share, outstanding.

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**PART I - FINANCIAL INFORMATION**

**Item 1. Condensed Consolidated Financial Statements (Unaudited).**

**KARYOPHARM THERAPEUTICS INC.**
**CONDENSED CONSOLIDATED BALANCE SHEETS**
**(unaudited)**
**(in thousands, except per share amounts)**

| | March 31, 2024 | December 31, 2023 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 30,628 | $ 52,231 |
| Investments | 117,950 | 139,212 |
| Accounts receivable, net | 31,082 | 26,962 |
| Inventory | 2,769 | 3,043 |
| Prepaid expenses and other current assets | 15,478 | 11,813 |
| Restricted cash | 459 | 660 |
| Total current assets | 198,366 | 233,921 |
| Property and equipment, net | 719 | 606 |
| Operating lease right-of-use assets | 3,735 | 4,276 |
| Restricted cash | 304 | 301 |
| Other assets | 1,334 | 1,334 |
| Total assets | $ 204,458 | $ 240,438 |
| **Liabilities and stockholders' deficit** | | |
| Current liabilities: | | |
| Accounts payable | $ 5,028 | $ 3,123 |
| Accrued expenses | 54,851 | 61,394 |
| Operating lease liabilities | 3,425 | 3,308 |
| Other current liabilities | 2,037 | 1,654 |

| | | |
|---|---|---|
| Total current liabilities | 65,341 | 69,479 |
| Convertible senior notes | 171,127 | 170,919 |
| Deferred royalty obligation | 132,479 | 132,479 |
| Operating lease liabilities, net of current portion | 1,884 | 2,789 |
| Other liabilities | 2,582 | 978 |
| Total liabilities | 373,413 | 376,644 |
| Stockholders' deficit: | | |
| Preferred stock, $ 0.0001 par value; 5,000 shares authorized; none issued and outstanding | — | — |
| Common stock, $ 0.0001 par value; 400,000 shares authorized; 116,457 and 114,915 shares issued and outstanding at March 31, 2024 and December 31, 2023, respectively | 12 | 12 |
| Additional paid-in capital | 1,355,951 | 1,350,981 |
| Accumulated other comprehensive loss | (518) | (161) |
| Accumulated deficit | (1,524,400) | (1,487,038) |
| Total stockholders' deficit | (168,955) | (136,206) |

| | | |
|---|---|---|
| Total liabilities and stockholders' deficit | 204,458 | 240,438 |
| | $ | $ |

See accompanying notes to condensed consolidated financial statements.

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**KARYOPHARM THERAPEUTICS INC.**
**CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS**
**(unaudited)**
**(in thousands, except per share amounts)**

| | For the Three Months Ended March 31, | |
|---|---|---|
| | 2024 | 2023 |
| Revenues: | | |
| Product revenue, net | $ 26,006 | $ 28,288 |
| License and other revenue | 7,120 | 10,410 |
| Total revenue | 33,126 | 38,698 |
| Operating expenses: | | |
| Cost of sales | 1,911 | 1,351 |
| Research and development | 35,425 | 32,339 |
| Selling, general and administrative | 29,549 | 35,907 |
| Total operating expenses | 66,885 | 69,597 |
| Loss from operations | ( 33,759 ) | ( 30,899 ) |
| Other income (expense): | | |
| Interest income | 2,156 | 2,849 |
| Interest expense | ( 5,884 ) | ( 5,758 ) |
| Other income (expense), net | 196 | ( 264 ) |
| Total other expense, net | ( 3,532 ) | ( 3,173 ) |
| Loss before income taxes | ( 37,291 ) | ( 34,072 ) |
| Income tax provision | ( 71 ) | ( 54 ) |
| Net loss | $ ( 37,362 ) | $ ( 34,126 ) |
| Net loss per share—basic and diluted | $ ( 0.32 ) | $ ( 0.30 ) |

| | | |
|---|---|---|
| Weighted-average number of common shares outstanding used to compute net loss per share—basic and diluted | 115,454 | 113,481 |

See accompanying notes to condensed consolidated financial statements.

**KARYOPHARM THERAPEUTICS INC.**
**CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS**
**(unaudited)**
**(in thousands)**

| | For the Three Months Ended March 31, | |
|---|---|---|
| | 2024 | 2023 |
| Net loss | $ (37,362) | $ (34,126) |
| Other comprehensive (loss) income | | |
| Unrealized (loss) gain on investments | (39) | 33 |
| Foreign currency translation adjustment | (318) | 186 |
| Comprehensive loss | $ (37,719) | $ (33,907) |

See accompanying notes to condensed consolidated financial statements.

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**KARYOPHARM THERAPEUTICS INC.**
**CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS**
**(unaudited)**
**(in thousands)**

| | For the Three Months Ended March 31, | |
|---|---|---|
| | 2024 | 2023 |
| **Operating activities** | | |
| Net loss | $ (37,362) | $ (34,126) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Stock-based compensation expense | 4,970 | 5,389 |
| Depreciation and amortization | 85 | 290 |
| Amortization of debt issuance costs | 208 | 201 |
| Net amortization of premiums and discounts on investments | (911) | (1,126) |
| Other | — | 4 |
| Changes in operating assets and liabilities: | | |
| Accounts receivable, net | (4,120) | 11,886 |
| Inventory | 274 | 397 |
| Prepaid expenses and other assets | (3,665) | 1,537 |
| Operating lease right-of-use assets | 541 | 462 |
| Accounts payable | 1,905 | 6,272 |
| Accrued expenses and other liabilities | (4,862) | (9,414) |
| Operating lease liabilities | (788) | (682) |
| Net cash used in operating activities | (43,725) | (18,910) |
| **Investing activities** | | |
| Proceeds from maturities of investments | 53,743 | 27,944 |
| Purchases of investments | (31,608) | (60,332) |
| Purchases of property and equipment | (195) | — |

| | | |
|---|---|---|
| Net cash provided by (used in) investing activities | 21,940 | ( 32,388 ) |
| Effect of exchange rate on cash, cash equivalents and restricted cash | ( 16 ) | ( 45 ) |
| Net decrease in cash, cash equivalents and restricted cash | ( 21,801 ) | ( 51,343 ) |
| Cash, cash equivalents and restricted cash at beginning of period | 53,192 | 136,885 |
| Cash, cash equivalents and restricted cash at end of period | $ 31,391 | $ 85,542 |
| **Reconciliation of cash, cash equivalents and restricted cash reported within the condensed consolidated balance sheets** | | |
| Cash and cash equivalents | $ 30,628 | $ 84,062 |
| Short-term restricted cash | 459 | 846 |
| Long-term restricted cash | 304 | 634 |
| Total cash, cash equivalents and restricted cash | $ 31,391 | $ 85,542 |
| Supplemental disclosures: | | |
| Cash paid for amounts included in the measurement of operating lease liabilities | $ 948 | $ 923 |
| Cash paid for interest on deferred royalty obligation | $ 4,103 | $ 4,076 |

See accompanying notes to condensed consolidated financial statements.

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**KARYOPHARM THERAPEUTICS INC.**
**CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' DEFICIT**
**(unaudited)**
**(in thousands)**

| | Common Shares | | Additional Paid-In Capital | Accumulated Other Comprehensive (Loss) Income | Accumulated Deficit | Total Stockholders' Deficit |
|---|---|---|---|---|---|---|
| | Shares | Amount | | | | |
| **Balance at December 31, 2023** | 114,915 | $ 12 | $ 1,350,981 | $ (161) | $ (1,487,038) | $ (136,206) |
| Vesting of restricted stock | 1,542 | — | — | — | — | — |
| Stock-based compensation expense | — | — | 4,970 | — | — | 4,970 |
| Unrealized loss on investments | — | — | — | (39) | — | (39) |
| Foreign currency cumulative translation adjustment | — | — | — | (318) | — | (318) |
| Net loss | — | — | — | — | (37,362) | (37,362) |
| **Balance at March 31, 2024** | 116,457 | $ 12 | $ 1,355,951 | $ (518) | $ (1,524,400) | $ (168,955) |
| **Balance at December 31, 2022** | 113,213 | $ 12 | $ 1,327,909 | $ (638) | $ (1,343,939) | $ (16,656) |
| Vesting of restricted stock | 758 | — | — | — | — | — |
| Stock-based compensation expense | — | — | 5,389 | — | — | 5,389 |
| Unrealized gain on investments | — | — | — | 33 | — | 33 |
| Foreign currency cumulative translation adjustment | — | — | — | 186 | — | 186 |
| Net loss | — | — | — | — | (34,126) | (34,126) |
| **Balance at March 31, 2023** | 113,971 | $ 12 | $ 1,333,298 | $ (419) | $ (1,378,065) | $ (45,174) |

See accompanying notes to condensed consolidated financial statements.

**KARYOPHARM THERAPEUTICS INC.**
**NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS**

## 1. Nature of Business and Basis of Presentation

### *Nature of Business*

Karyopharm Therapeutics Inc., a Delaware corporation (collectively with its subsidiaries, the "Company," "we," "us," or "our"), is a commercial-stage pharmaceutical company pioneering novel cancer therapies and dedicated to the discovery, development and commercialization of first-in-class drugs directed against nuclear export for the treatment of cancer and other diseases. We were incorporated in Delaware on December 22, 2008 and have a principal place of business in Newton, Massachusetts.

Our scientific expertise is based upon an understanding of the regulation of intracellular communication between the nucleus and the cytoplasm. We have discovered and are developing and commercializing novel, small molecule Selective Inhibitor of Nuclear Export compounds that inhibit the nuclear export protein exportin 1. Our primary focus is on marketing XPOVIO® (selinexor) in its currently approved indications, as well as developing and seeking regulatory approval of selinexor as an oral agent targeting multiple high unmet cancer indications, including our core programs in endometrial cancer, multiple myeloma, and myelofibrosis.

Our lead asset, XPOVIO, received its initial U.S. approval from the U.S. Food and Drug Administration (the "FDA") in July 2019 and is currently approved and marketed for the following indications: (i) in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy; (ii) in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody; and (iii) for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma ("DLBCL"), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least two lines of systemic therapy. The commercialization of XPOVIO and NEXPOVIO (the brand name for selinexor in Europe and the United Kingdom) outside of the U.S. is managed by our partners in their respective territories. XPOVIO/NEXPOVIO has received regulatory approval in various indications in over 40 countries outside the U.S. and is commercially available in a growing number of countries as our partners continue to secure reimbursement approvals.

### *Basis of Presentation*

The accompanying unaudited condensed consolidated financial statements of the Company have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP") for interim financial reporting and as required by Regulation S-X, Rule 10-01. Accordingly, they do not include all of the information and footnotes required by GAAP for complete financial statements. In the opinion of management, all adjustments (including those which are normal and recurring) considered necessary for a fair presentation of the interim financial information have been included. When preparing financial statements in conformity with GAAP, we must make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues, expenses and related disclosures at the date of the financial statements. Actual results could differ from those estimates. Additionally, operating results for the three months ended March 31, 2024 are not necessarily indicative of the results that may be expected for any other interim period or for the fiscal year ending December 31, 2024. For further information, refer to the financial statements and footnotes included in our Annual Report on Form 10-K for the year ended December 31, 2023 as filed with the Securities and Exchange Commission on February 29, 2024 ("Annual Report").

### *Basis of Consolidation*

The condensed consolidated financial statements at March 31, 2024 include the accounts of Karyopharm Therapeutics Inc. and its wholly-owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

The significant accounting policies used in preparation of these condensed consolidated financial statements in this Form 10-Q are consistent with those discussed in Note 2, "*Summary of Significant Accounting Policies*," in our Annual Report.

**2. Product Revenue**

To date, our only source of product revenue has been from the U.S. sales of XPOVIO. Net product revenue, including provisions primarily consisting of distribution fees and cash discounts, as well as reserves for chargebacks, rebates and returns, were as follows (in thousands):

| | For the Three Months Ended March 31, | |
|---|---|---|
| | 2024 | 2023 |
| Gross product revenue | $ 36,763 | $ 37,065 |
| Provisions for product revenue | ( 10,757 ) | ( 8,777 ) |
| Total product revenue, net | $ 26,006 | $ 28,288 |

As of March 31, 2024 and December 31, 2023, net product revenue of $ 23.1 million and $ 17.8 million, respectively, were included in accounts receivable. To date, we have had no bad debt write-offs and we do not currently have credit issues with any customers. There were no credit losses associated with accounts receivable as of March 31, 2024 and December 31, 2023.

**3. Inventory**

The following table presents our inventory (in thousands), all of which was related to XPOVIO:

| | As of March 31, 2024 | As of December 31, 2023 |
|---|---|---|
| Raw materials | $ 553 | $ 553 |
| Work in process | 1,589 | 1,732 |
| Finished goods | 627 | 758 |
| Total inventory | $ 2,769 | $ 3,043 |

XPOVIO was initially approved by the FDA in July 2019 at which time we began to capitalize costs to manufacture XPOVIO.

**4. License Agreements**

In prior periods, we entered into license agreements with Berlin-Chemie AG, an affiliate of the Menarini Group ("Menarini") and Antengene Therapeutics Limited ("Antengene"), both of which are accounted for within the scope of Accounting Standards Codification 606, *Revenue from Contracts with Customers.* For further details on the terms and accounting treatment considerations for these contracts, please refer to Note 5, "*License and Asset Purchase Agreements*," to our consolidated financial statements contained in Item 8 of our Annual Report.

The following table presents information about our license and other revenue (in thousands):

| | For the Three Months Ended March 31, | |
|---|---|---|
| | 2024 | 2023 |
| Menarini | $ 6,406 | $ 8,737 |

| | | |
|---|---|---|
| Antengene | | |
| | 511 | 1,112 |
| Other | | |
| | 203 | 561 |
| Total license and other revenue | | |
| | $ 7,120 | $ 10,410 |

During the three months ended March 31, 2024, we recognized $

5.8
million of revenue for the reimbursement of development-related expenses from Menarini.

During the three months ended March 31, 2023, we recognized $

4.8
million of revenue for the reimbursement of development-related expenses and $

3.5
million of license-related revenue from Menarini.

At March 31, 2024, license and other revenue of $

8.0
million and $

1.0
million were included in accounts receivable and other current assets, respectively. At December 31, 2023, license and other revenue of $

9.1
million and $

1.0
million were included in accounts receivable and other current assets, respectively.

**5. Fair Value Measurements**

Financial instruments, including cash, cash equivalents, accounts receivable, net, other current assets, other assets, restricted cash, accounts payable, and accrued expenses, are presented at amounts that approximate fair value at March 31, 2024 and December 31, 2023.

Fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. We disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. The fair value hierarchy prioritizes valuation inputs based on the observable nature of those inputs. The fair value hierarchy applies only to the valuation inputs used in determining the reported fair value and is not a measure of credit quality. The hierarchy defines three levels of valuation inputs:

Level 1 - Quoted prices in active markets for identical assets or liabilities

Level 2 - Inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly

Level 3 - Unobservable inputs that reflect the assumptions market participants would use in pricing the asset or liability

Items classified as Level 2 consist of corporate debt securities, commercial paper and U.S. government and agency securities. We estimate the fair value of these marketable securities by taking into consideration valuations obtained from third-party pricing sources. These pricing sources utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include market pricing based on real-time trade data for the same or similar securities, issuer credit spreads, benchmark yields, and other observable inputs. We validate the prices provided by our third-party pricing sources by understanding the models used, obtaining market values from other pricing sources and analyzing pricing data in certain instances.

In certain cases where there is limited activity or less transparency around inputs to valuation, the related assets or liabilities are classified as Level 3. The embedded derivative liability associated with a Revenue Interest Financing Agreement (the “Revenue Interest Agreement”) we entered into with HealthCare Royalty Partners III, L.P. and HealthCare Royalty Partners IV, L.P. (“HCRx”) in September 2019 and as amended in June 2021 and August 2023 (as amended, the “Amended Revenue Interest Agreement”), as discussed further in Note 10, “*Long-Term Obligations*”, is measured at fair value and is included as a component of the deferred royalty obligation on our condensed consolidated balance sheets. The embedded derivative liability is subject to remeasurement at the end of each reporting period, with changes in fair value recognized as a component of other income (expense), net on the condensed consolidated statements of operations. The valuation method incorporates certain unobservable Level 3 key inputs including: (i) the probability-weighted net sales of XPOVIO and any of our other future products, including worldwide net product sales, upfront payments, milestones and royalties; (ii) our risk-adjusted discount rate; and (iii) the probability of a change in control occurring during the term of the instrument.

The following tables present information about our financial assets and liability that have been measured at fair value and indicate the fair value hierarchy of the valuation inputs utilized to determine such fair value (in thousands):

| Description | As of March 31, 2024 | Quoted Prices in Active Markets for Identical Assets (Level 1) | Significant Other Observable Inputs (Level 2) | Significant Unobservable Inputs (Level 3) |
|---|---|---|---|---|
| **Financial assets** | | | | |
| Cash equivalents: | | | | |
| Money market funds | $ 8,535 | $ 8,535 | $ — | $ — |
| Commercial paper | 1,490 | — | 1,490 | — |
| U.S. government and agency securities | 4,045 | — | 4,045 | — |
| Investments: | | | | |
| Corporate debt securities | 89,356 | — | 89,356 | — |
| Commercial paper | 13,626 | — | 13,626 | — |
| U.S. government and agency securities | 14,968 | — | 14,968 | — |
| | $ 132,020 | $ 8,535 | $ 123,485 | $ — |
| **Financial liability** | | | | |
| Embedded derivative liability | $ 2,800 | $ — | $ — | $ 2,800 |

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| Description | As of December 31, 2023 | Quoted Prices in Active Markets for Identical Assets (Level 1) | Significant Other Observable Inputs (Level 2) | Significant Unobservable Inputs (Level 3) |
|---|---|---|---|---|
| **Financial assets** | | | | |
| Cash equivalents: | | | | |
| Money market funds | $ 27,963 | $ 27,963 | $ — | $ — |
| U.S. government and agency securities | 1,998 | — | 1,998 | — |
| Investments: | | | | |
| Corporate debt securities | 77,961 | — | 77,961 | — |
| Commercial paper | 13,744 | — | 13,744 | — |
| U.S. government and agency securities | 47,507 | — | 47,507 | — |
| | $ 169,173 | $ 27,963 | $ 141,210 | $ — |
| **Financial liability** | | | | |
| Embedded derivative liability | $ 2,800 | $ — | $ — | $ 2,800 |

**6. Investments**

The following tables summarize our investments, which are classified as available-for-sale and recorded at fair value (in thousands):

| | As of March 31, 2024 | | | |
|---|---|---|---|---|
| | Amortized Cost | Total Unrealized Gains | Total Unrealized Loss | Aggregate Fair Value |
| Corporate debt securities | $ 89,444 | $ 27 | $ (115) | $ 89,356 |
| Commercial paper | 13,639 | 3 | (16) | 13,626 |
| U.S. government and agency securities | 14,974 | — | (6) | 14,968 |
| Total | $ 118,057 | $ 30 | $ (137) | $ 117,950 |

| | As of December 31, 2023 | | | |
|---|---|---|---|---|
| | Amortized Cost | Total Unrealized Gains | Total Unrealized Loss | Aggregate Fair Value |
| Corporate debt securities | $ 78,004 | $ 79 | $ (122) | $ 77,961 |
| Commercial paper | 13,734 | 13 | (3) | 13,744 |

| | | | | |
|---|---|---|---|---|
| U.S. government and agency securities | 47,543 | 4 | (40) | 47,507 |
| Total | $ 139,281 | $ 96 | $ (165) | $ 139,212 |

We determine the appropriate classification of our investments at the time of purchase. All of our investments are reported as short-term as they are available for use during the normal cycle of business. We review any investment when its fair value is less than its amortized cost and when evidence indicates that the investment's carrying amount is not recoverable within a reasonable period. We evaluate whether the decline in fair value has resulted from credit losses or other factors. In making this assessment, we consider the extent to which fair value is less than amortized cost, any changes to the rating of the security by a rating agency, and adverse conditions specifically related to the security, among other factors. If this assessment indicates that a credit loss exists, the present value of cash flows expected to be collected from the investment is compared to its amortized cost basis. If the present value of cash flows expected to be collected is less than the amortized cost basis, a credit loss exists and an allowance for credit losses is recorded on our condensed consolidated balance sheet, limited by the amount that the fair value is less than the amortized cost basis. Any impairment that is not related to a credit loss is recognized in other comprehensive (loss) income.

Changes in the allowance for credit losses are recorded as a provision for (or reversal of) credit loss expense. Losses are charged against the allowance when we believe the uncollectability of an investment is confirmed or when either of the criteria regarding intent or requirement to sell is met. We held

55
and

41
debt securities at March 31, 2024 and December 31, 2023, respectively, that were in an unrealized loss position. The unrealized losses at March 31, 2024 and December 31, 2023 were attributable to changes in interest rates, and we do

no

t believe any unrealized losses represent credit losses.

We do not intend to sell the investments before recovery of their amortized cost bases, which may be at maturity. All of our investments mature within two years from March 31, 2024. The following tables summarize our investments in an unrealized loss position for which an allowance for credit losses has not been recorded, aggregated by investment type and length of time in a continuous unrealized loss position (in thousands):

| | As of March 31, 2024 | | | | | |
|---|---|---|---|---|---|---|
| | Less than 12 Months | | 12 Months or Longer | | Total | |
| | Aggregate Related Fair Value | Unrealized Losses | Aggregate Related Fair Value | Unrealized Losses | Aggregate Related Fair Value | Unrealized Losses |
| Corporate debt securities | $ 69,829 | $ (105) | $ 6,851 | $ (10) | $ 76,680 | $ (115) |
| Commercial paper | 10,703 | (16) | — | — | 10,703 | (16) |
| U.S. government and agency securities | 12,968 | (5) | 2,000 | (1) | 14,968 | (6) |
| Total | $ 93,500 | $ (126) | $ 8,851 | $ (11) | $ 102,351 | $ (137) |

| | As of December 31, 2023 | | | | | |
|---|---|---|---|---|---|---|
| | Less than 12 Months | | 12 Months or Longer | | Total | |
| | Aggregate Related Fair Value | Unrealized Losses | Aggregate Related Fair Value | Unrealized Losses | Aggregate Related Fair Value | Unrealized Losses |
| Corporate debt securities | $ 50,322 | $ (112) | $ 4,279 | $ (10) | $ 54,601 | $ (122) |
| Commercial paper | 6,952 | (3) | — | — | 6,952 | (3) |
| U.S. government and agency securities | 27,191 | (37) | 1,997 | (3) | 29,188 | (40) |
| Total | $ 84,465 | $ (152) | $ 6,276 | $ (13) | $ 90,741 | $ (165) |

**7. Net Loss Per Share**

Basic net loss per common share is calculated by dividing net loss by the weighted-average number of common shares outstanding for the period. Diluted net loss per common share is calculated by dividing the diluted net loss by the weighted average number of common shares outstanding, including potential dilutive common shares assuming the dilutive effect of outstanding stock options and unvested restricted stock units. For periods in which we have reported net losses, diluted net loss per common share is the same as basic net loss per common share, since dilutive common shares are not included if their effect is anti-dilutive.

The following potentially dilutive securities were excluded from the calculation of diluted net loss per common share due to their anti-dilutive effect (in thousands):

| | As of March 31, | |
|---|---|---|
| | 2024 | 2023 |
| Outstanding stock options | 8,472 | 11,851 |
| Unvested restricted stock units | 12,775 | 8,085 |

As discussed further in Note 10, “*Long-Term Obligations*”, we have the option to settle the conversion obligation for our

3.00
% convertible senior notes due 2025 (the “2025 Notes”) in cash, shares or any combination of the two. Based on our net loss position, there was no impact on the calculation of dilutive loss per common share during the three months ended March 31, 2024 and 2023.

As discussed further in Note 9, “*Stockholders’ Equity*”, warrants to purchase up to

9,787,563
shares of our common stock are outstanding as of March 31, 2024. These warrants were excluded from the calculation of basic and diluted net loss per common share during the three months ended March 31, 2024 and 2023 as the warrant holders do not have an obligation to share in our losses.

**8. Stock-based Compensation Expense**

The following table summarizes stock-based compensation expense included in operating expenses (in thousands):

| | For the Three Months Ended March 31, | |
|---|---|---|
| | 2024 | 2023 |
| Cost of sales | $ 54 | $ 81 |
| Research and development | 1,421 | 1,938 |
| Selling, general and administrative | 3,495 | 3,370 |
| Total | $ 4,970 | $ 5,389 |

**9. Stockholders' Equity**

***Common Share Warrants***

On December 5, 2022, we issued to certain institutional investors, in a private placement offering of securities, warrants to purchase up to

9,537,563

shares of common stock at an exercise price of $

6.36

per share. The warrants are exercisable through December 7, 2027. As of March 31, 2024,

no

ne of these warrants have been exercised.

On August 1, 2023, in connection with the Second Amendment to the Revenue Interest Agreement dated as of August 1, 2023, we issued warrants to HCRx to purchase up to

250,000

shares of common stock at an exercise price of $

2.25

per share. The warrants are exercisable through August 1, 2030. As of March 31, 2024,

no

ne of these warrants have been exercised.

***Open Market Sale Agreement***

On February 17, 2023, we entered into an Open Market Sale Agreement (the "2023 Open Market Sale Agreement") with Jefferies LLC, as agent ("Jefferies"). Under the 2023 Open Market Sale Agreement, we may issue and sell shares of our common stock having an aggregate offering price of up to $

100.0

million (the "Shares") from time to time through Jefferies (the "2023 Open Market Offering").

Under the 2023 Open Market Sale Agreement, Jefferies may sell the Shares by methods deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended (the "Securities Act"). We may sell the Shares in amounts and at times to be determined by us from time to time subject to the terms and conditions of the 2023 Open Market Sale Agreement, but we have no obligation to sell any of the Shares in the 2023 Open Market Offering.

We or Jefferies may suspend or terminate the offering of Shares upon notice to the other party and subject to other conditions. We have agreed to pay Jefferies commissions for its services in acting as agent in the sale of the Shares in the amount of up to

3.0

% of gross proceeds from the sale of the Shares pursuant to the 2023 Open Market Sale Agreement. We have also agreed to provide Jefferies with customary indemnification and contribution rights.

We did

no

t sell any Shares under the 2023 Open Market Sale Agreement during the three months ended March 31, 2024 and 2023. As of March 31, 2024, $

100.0

million of Shares was available for issuance and sale under the 2023 Open Market Sale Agreement.

**10. Long-Term Obligations**

***3.00% Convertible Senior Notes due 2025***

On October 16, 2018, we completed an offering of $

150.0

million aggregate principal amount of the 2025 Notes. In addition, on October 26, 2018, we issued an additional $

22.5

million aggregate principal amount of the 2025 Notes pursuant to the full exercise of the option to purchase additional 2025 Notes granted to the initial purchasers in the offering. The 2025 Notes were sold in a private offering to qualified institutional buyers in reliance on Rule 144A under the Securities Act. In connection with the issuance of the 2025 Notes, we incurred approximately $

5.6

million of debt issuance costs, which primarily consisted of underwriting, legal and other professional fees. Debt issuance costs are being amortized to interest expense using the effective interest method over seven years .

The 2025 Notes are senior unsecured obligations and bear interest at a rate of

3.00

% per year payable semiannually in arrears on April 15 and October 15 of each year, beginning on April 15, 2019. Upon conversion, the 2025 Notes

will be converted into cash, shares of our common stock, or a combination of cash and shares of our common stock, at our election. As of October 15, 2022, the 2025 Notes are subject to redemption at our option, in whole or in part, if the conditions described below are satisfied. Holders may require us to repurchase their 2025 Notes following a fundamental change (as defined within the indenture governing the 2025 Notes) at a cash repurchase price generally equal to the principal amount of the 2025 Notes to be repurchased, plus accrued and unpaid interest. The 2025 Notes will mature on October 15, 2025 , unless earlier converted, redeemed or repurchased in accordance with their terms. Subject to satisfaction of certain conditions and during the periods described below, the 2025 Notes may be converted at an initial conversion rate of

63.0731
shares of common stock per $

1,000
principal amount of the 2025 Notes (equivalent to an initial conversion price of approximately $

15.85
per share of common stock).

Holders of the 2025 Notes may convert all or any portion of their 2025 Notes, in multiples of $

1,000
principal amount, at their option at any time prior to the close of business on the business day immediately preceding June 15, 2025 only under the following circumstances:

(1) during any calendar quarter commencing after the calendar quarter ending on December 31, 2018 (and only during such calendar quarter), if the last reported sale price of our common stock for at least

20
trading days (whether or not consecutive) during the period of

30
consecutive trading days ending on, and including, the last trading day of the immediately preceding calendar quarter is greater than or equal to

130
% of the conversion price for the 2025 Notes on each applicable trading day;

(2) during the five-business day period immediately after any

five
consecutive trading day period (the “Measurement Period”) in which the trading price per $

1,000
principal amount of 2025 Notes for each trading day of the Measurement Period was less than

98
% of the product of the last reported sale price of our common stock and the conversion rate on each such trading day;

(3) if we call the 2025 Notes for redemption, until the close of business on the business day immediately preceding the redemption date; or

(4) upon the occurrence of specified corporate events as described within the indenture governing the 2025 Notes.

As of March 31, 2024, none of the above circumstances had occurred and as such, the 2025 Notes could not have been converted.

As of October 15, 2022, we may redeem for cash all or part of the 2025 Notes at our option if the last reported sale price of our common stock equals or exceeds

130
% of the conversion price then in effect for at least

20
trading days (whether or not consecutive) during any

30
consecutive trading day period ending within five trading days prior to the date on which we send any notice of redemption. The redemption price will be

100
% of the principal amount of the 2025 Notes to be redeemed, plus accrued and unpaid interest, if any. In addition, calling any convertible note for redemption will constitute a make-whole fundamental change with respect to that convertible note, in which case the conversion rate applicable to the conversion of that convertible note, if it is converted in connection with the redemption, will be increased in certain circumstances. We did not redeem any of the 2025 Notes as of March 31, 2024.

The outstanding balances of the 2025 Notes consisted of the following (in thousands):

| | As of March 31, 2024 | As of December 31, 2023 |
|---|---|---|
| Principal | $ 172,500 | $ 172,500 |
| Less: debt issuance costs | ( 1,373 ) | ( 1,581 ) |
| Net carrying amount | $ 171,127 | $ 170,919 |

We determined the expected life of the 2025 Notes was equal to its seven-year term and the effective interest rate was

3.53
%. As of March 31, 2024, the “if-converted value” did not exceed the remaining principal amount of the 2025 Notes. The fair value of the 2025 Notes was determined based on data points other than quoted prices that are observable, either directly or indirectly, and has been classified as Level 2 within the fair value hierarchy. The fair value of the 2025 Notes, which differs from their carrying value, is influenced by market interest rates, our stock price and stock price volatility. The estimated fair value of the 2025 Notes as of March 31, 2024 and December 31, 2023 was approximately $

93.0
million and $

87.9
million, respectively.

The following table sets forth total interest expense recognized related to the 2025 Notes (in thousands):

| | For the Three Months Ended March 31, | |
|---|---|---|
| | 2024 | 2023 |
| Contractual interest expense | $ 1,294 | $ 1,294 |
| Amortization of debt issuance costs | 208 | 201 |
| Total | $ 1,502 | $ 1,495 |

Future minimum payments on the 2025 Notes as of March 31, 2024 were as follows (in thousands):

| Years ended December 31, | Future Minimum Payments |
|---|---|
| 2024 | $ 5,175 |
| 2025 | 177,675 |
| Total minimum payments | 182,850 |
| Less: interest expense and issuance costs | ( 11,723 ) |
| Convertible senior notes | $ 171,127 |

Following completion of the transactions discussed below under "*Refinance of Long-Term Obligations*," we expect that $

24.5

million aggregate principal amount of Notes will remain outstanding.

***Deferred Royalty Obligation***

In September 2019, we entered into the Revenue Interest Agreement with HCRx, which was subsequently amended in June 2021 and August 2023. We received $

75.0

million, less certain transaction expenses, upon closing of the Revenue Interest Agreement (the "First Investment Amount") and $

60.0

million in June 2021 (the "Second Investment Amount" and together with the First Investment Amount, the "Investment Amounts").

In exchange for the above payments, HCRx receives payments from us at a tiered percentage (the "Applicable Tiered Percentage") of net revenues of selinexor and any of our other future products, including worldwide net product sales and upfront payments, milestones, and royalties. The Applicable Tiered Percentage is subject to reduction in the future if a target based on cumulative U.S. net sales of selinexor is met. Total payments to HCRx are capped at

195

% of the Investment Amounts (the "Payment Cap"). As described in more detail below, as of May 2024, HCRx will receive payments from us at a fixed royalty percentage for the remainder of the Revenue Interest Agreement, as amended.

If HCRx has not received

100

% of the First Investment Amount and

65

% of the Second Investment Amount by June 30, 2025 (the "First Minimum Aggregate Payment"), or

100

% of both the First Investment Amount and the Second Investment Amount by September 30, 2026, we must make a cash payment sufficient to gross up the payments to such minimum amounts. As described in more detail below, HCRx received

100

% of the First Investment Amount and Second Investment Amount in May 2024 and as such, these gross payments are no longer applicable.

As the repayment of the funded amount is contingent upon worldwide net product sales and upfront payments, milestones, and royalties, the repayment term may be shortened or extended depending on actual worldwide net product sales and upfront payments, milestones, and royalties. The repayment period commenced on October 1, 2019 for the First Investment Amount and on July 1, 2021 for the Second Investment Amount, and expires on the earlier of (i) the date in which HCRx has received cash payments totaling an aggregate of

195

% of the Investment Amounts or (ii) the legal maturity date of October 1, 2031. If HCRx has not received payments equal to

195

% of the Investment Amounts by the twelve-year anniversary of the initial closing date, we will be required to pay an amount equal to the Investment Amounts plus a specific annual rate of return less payments previously paid to HCRx. In the event of a change of control, we are obligated to pay HCRx an amount equal to

195

% of the Investment Amounts less payments previously paid to HCRx. In addition, upon the occurrence of an event of default, including, among others, our failure to pay any amounts due to HCRx, insolvency, our failure to pay indebtedness when due, the revocation of regulatory approval of XPOVIO in the U.S. or our breach of any covenant contained in the Amended Revenue Interest Agreement and our failure to cure the breach within the prescribed time frame, we are obligated to pay HCRx an amount equal to

195

% of the Investment Amounts less payments previously paid to HCRx. In addition, upon an event of default, HCRx may exercise all other rights and remedies available under the Amended Revenue Interest Agreement, including foreclosing on the collateral that was pledged to HCRx, which consists of all of our present and future assets. As of March 31, 2024, we have made $

65.8

million in payments to HCRx.

We have evaluated the terms of the Amended Revenue Interest Agreement and concluded that the features of both the First Investment Amount and Second Investment Amount are similar to those of a debt instrument. Accordingly, we have accounted for the transaction as long-term debt and presented it as a deferred royalty obligation on our condensed consolidated balance sheets.

We have also determined that the repayment of

195

% of the Investment Amounts, less any payments made to date, upon a change of control is an embedded derivative that requires bifurcation from the debt instrument and fair value recognition as further described in Note 5, "*Fair Value Measurements"* to our condensed consolidated financial statements.

The effective interest rate as of March 31, 2024 was approximately

14
%. We have incurred debt issuance costs totaling $

1.7
million. Debt issuance costs have been netted against the debt and are being amortized over the estimated term of the debt using the effective interest method, adjusted on a prospective basis for changes in the underlying assumptions and inputs.

The carrying value of the deferred royalty obligation at both March 31, 2024 and December 31, 2023 was $

129.7

million, based on $

135.0

million of proceeds, net of the fair value of the bifurcated embedded derivative liability upon receipt of the First Investment Amount and Second Investment Amount, and debt issuance costs incurred. The carrying value of the deferred royalty obligation approximated fair value at March 31, 2024 and December 31, 2023 and is based on our current estimates of future payments to HCRx over the life of the arrangement, which are considered Level 3 inputs.

***Refinance of Long-Term Obligations***

On May 8, 2024, we entered into a series of transactions to limit our aggregate indebtedness, extend the maturity of certain of our indebtedness and provide us with additional working capital. As described in more detail below we:

(1) Borrowed $

85.0
million from existing holders of our 2025 Notes and $

15.0
million from HCRx under a $

100.0
million senior secured term loan facility (the "Term Loan").

(2) Entered into agreements to exchange approximately $

148.0
million aggregate principal amount of our 2025 Notes for (i) approximately $

111.0
million aggregate principal amount of our newly issued

6.00
% secured Convertible Senior Notes due 2029 (the "2029 Notes") and (ii) warrants to purchase up to 45.8 million shares of our common stock (the "Warrants"). Closing of these transactions is expected to occur on or around May 13, 2024, subject to customary closing conditions.

(3) Entered into an amendment to the Amended Revenue Interest Agreement with HCRx (the "HCRx Amendment" and as further amended in May 2024, the "Amended Revenue Interest Agreement") that, among other things, (i) acknowledges that aggregate payments to HCRx will equal $

135.0
million after the refinancing transactions are complete, (ii) subordinates the indebtedness and liens under the Amended Revenue Interest Agreement to the indebtedness and liens under the Term Loan, and (iii) modifies the Applicable Tiered Percentage for the remainder of the payments we will make to HCRx under the Amended Revenue Interest Agreement.

*Credit Agreement and Term Loan*

On May 8, 2024 (the "Closing Date"), we entered into a credit and guaranty agreement (the "Credit Agreement") with certain existing holders of the 2025 Notes and HCRx, which provides for a senior secured term loan facility of $

100.0
million. We will use the proceeds of the Term Loan to pay obligations under our Amended Revenue Interest Agreement with HCRx, for general corporate purposes and to pay fees and expenses in connection with the transactions described herein.

The Term Loan matures in May 2028 and bears interest at a variable rate equal to the applicable secured overnight financing rate plus

9.25
%, subject to a floor of

3.00
%. Principal payments under the Term Loan will begin in June 2026, and consist of quarterly cash payments in the amount of

6.25
% of the aggregate principal amount of the Term Loan, with the remaining principal due when the Term Loan matures in May 2028.

We can prepay the Term Loan at any time. All repayments, including prepayments, are subject to a redemption fee of

3.00
% of the principal paid. Prepayments made before May 8, 2027 are subject to a prepayment premium ranging from

3.00
% to

5.00
% of the principal prepaid. The prepayment premium for prepayments made before May 8, 2025 also includes the unpaid interest that would have accrued on the amount being prepaid through May 8, 2025. In addition, we are required to repay the Term Loan with proceeds from certain asset sales and condemnation events, subject, in some cases, to reinvestment rights.

All obligations under the Credit Agreement will be secured on a first priority basis, subject to certain exceptions, by substantially all of our assets. The Credit Agreement contains customary covenants, including a requirement to maintain cash, cash equivalents and investments of at least $

25.0
million at all times, and restrictions on indebtedness, liens, investments, fundamental changes, asset sales, licensing transactions, dividends, modifications to material agreements, payment of subordinated indebtedness, and other matters customarily restricted in such agreements. Specifically, we are prohibited from exclusively licensing, selling or otherwise disposing of U.S. rights to oncology indications of selinexor. If certain events of default occur, the Term Loan may be due and payable immediately. These events include the withdrawal of approval of certain indications of selinexor, payment defaults, covenant defaults, bankruptcy, cross-defaults to certain other agreements, change in control and lien priority.

*2029 Notes*

On the Closing Date, we also entered into privately-negotiated agreements (the "Exchange Agreements") with a limited number of existing holders of the 2025 Notes (the "Exchange Participants") to exchange approximately $

148.0
million aggregate principal amount of the Exchange Participants' existing 2025 Notes for (i) approximately $

111.0
million aggregate principal amount of the 2029 Notes and (ii) the Warrants to purchase up to 45.8 million shares of our common stock. The 2029 Notes and the Warrants are described in more detail below. Closing of the transactions pursuant to the Exchange Agreements is expected to occur on or around May 13, 2024, subject to customary closing conditions (the "2029 Notes Closing Date").

The 2029 Notes will be issued pursuant to an indenture (the "Indenture") under which we expect to issue $

116.0
million aggregate principal amount of the 2029 Notes on the 2029 Notes Closing Date, including $

111.0
million to the Exchange Participants and $

5.0
million to HCRx. The 2029 Notes will be second-lien secured obligations of the Company and bear interest at a rate of

6.00
% per year payable quarterly in arrears beginning on June 30, 2024. The 2029 Notes will mature on May 13, 2029, unless earlier converted, redeemed or repurchased in accordance with their terms.

The 2029 Notes will be convertible into shares of our common stock at an initial conversion rate of

444.4444
shares per $

1,000
principal amount, which is equivalent to a conversion price of $

2.25
per share and subject to adjustment upon the occurrence of certain events and customary anti-dilution adjustments. Upon conversion of the 2029 Notes, we will deliver shares of our common stock plus cash in lieu of any fractional shares to the holders of the 2029 Notes. Holders of the 2029 Notes may convert their 2029 Notes at any time prior to the close of business on May 13, 2029.

On or after May 13, 2026, we may redeem for cash all or a portion of the 2029 Notes if the last reported sale price of our common stock equals or exceeds

130
% of the conversion price then in effect for at least

20
trading days during any

30
consecutive trading day period. The redemption price will be equal to the principal amount of the 2029 Notes to be redeemed, plus any accrued and unpaid interest as of the redemption date. The redemption price will also include an amount equal to the aggregate value of all remaining interest payments on the 2029 Notes to be redeemed from the redemption date through maturity, which is payable in cash or, under certain circumstances and if we so elect, in shares of our common stock or a combination of cash and our common stock. Any shares of our common stock used to pay this amount will be valued based on their market price at the time of the redemption. In some cases, we will be required to make an offer to repurchase the 2029 Notes at a

101
% premium with proceeds from certain asset sales, subject, in some cases, to reinvestment rights.

If certain corporate events occur prior to the maturity date, a holder that elects to convert their 2029 Notes may be entitled to receive a payment from us, in cash or, under certain circumstances and if we so elect, in shares of our common stock, or a combination of cash and our common stock, based on an increase in the conversion rate in connection with such corporate event. In addition, if we undergo certain fundamental changes, holders may require us to repurchase for cash all or any portion of their 2029 Notes at a price equal to the principal amount of the 2029 Notes to be repurchased, plus any accrued and unpaid interest as of the repurchase date.

No holder will be entitled to receive shares of our common stock in connection with the 2029 Notes if such receipt would cause the holder (together with its affiliates) to own more than

4.99
% (subject to increase or decrease at the election of the holder, but in no event to exceed

19.99
%) of the number of shares of the common stock outstanding immediately after giving effect to such event. In addition, a holder may elect to receive pre-funded warrants with respect to any shares of common stock that would otherwise be issuable in connection with the 2029 Notes but for the foregoing ownership limitations. These pre-funded warrants will have an exercise price of $

0.0001
per share and will not expire.

All obligations under the 2029 Notes will be secured on a second priority basis by the same collateral that secures the obligations under the Term Loan. The 2029 Notes contain covenants and events of default that are generally consistent with the Term Loan.

*Warrants*

The exercise price of the Warrants to be issued will be $1.10 per share, subject to customary antidilution adjustments, and are exercisable at any time after their issuance and prior to May 13, 2029. If the closing price of our common stock exceeds two times the then current exercise price of the warrant for

20
trading days during any

30
consecutive trading day period, we can require the holder to exercise the warrant.

Under the terms of the Warrants, a holder cannot receive our common stock if such receipt would cause the holder (together with its affiliates) to own more than

4.99
% (subject to increase or decrease at the election of the holder, but in no event to exceed

19.99
%) of our common stock outstanding on the date of receipt. In addition, a holder may elect to receive pre-funded warrants with respect to any common stock that would otherwise be issuable but for the foregoing ownership limitations. These pre-funded warrants will have an exercise price of $

0.0001
per share and will not expire.

*HCRx Amendment*

On the Closing Date, we entered into the HCRx Amendment, pursuant to which we:

(1) made a cash payment to HCRx in the amount of approximately $

49.5
million,

(2) delivered to HCRx a Term Loan note with a principal amount of $

15.0
million, and

(3) agreed to deliver to HCRx 2029 Notes with a principal amount of $

5.0
million on or around May 13, 2024.

After giving effect to the above, we will have made aggregate payments under the Amended Revenue Interest Agreement totaling $

135.0
million. As a result, we will have no further gross-up payment obligations to HCRx, and the maximum remaining amount we owe to HCRx is $

128.3
million. After the Closing Date, we will make quarterly payments in the amount of a fixed percentage of our net product revenues, upfront payments, milestones, and royalties earned in the applicable quarter, subject to the provisions in the Amended Revenue Interest Agreement described earlier in this footnote.

The HCRx Amendment also subordinates the indebtedness and liens under the Amended Revenue Interest Agreement to the indebtedness and liens under the Term Loan, and, subject to certain exceptions, makes the indebtedness and liens under the Amended Revenue Interest Agreement pari passu with the indebtedness and liens under the 2029 Notes.

In addition, the HCRx Amendment reduces the exercise price of warrants to purchase shares of common stock issued to HCRx on August 1, 2023 from $

2.25
per share to $1.10 per share.

*Private Placement Shares to J. Wood Capital Advisors LLC*

We agreed with our financial advisor, J. Wood Capital Advisors LLC, to settle our financial advisory fee for services provided in connection with the transactions described above through the private placement of 6.9 million shares of our common stock.

**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 is meant to provide material information relevant to an assessment of the financial condition and results of operations of our company, including an evaluation of the amounts and uncertainties of cash flows from operations and from outside resources, so as to allow investors to better view our company from management's perspective. You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes appearing elsewhere in this quarterly report and the audited financial information and the notes thereto included in our Annual Report on Form 10-K for the year ended December 31, 2023, as filed with the Securities and Exchange Commission ("SEC") on February 29, 2024 ("Annual Report").*

**FORWARD-LOOKING STATEMENTS**

This Quarterly Report on Form 10-Q, contains forward-looking statements regarding the expectations of Karyopharm Therapeutics Inc., herein referred to as "Karyopharm," the "Company," "we," or "our," with respect to the possible achievement of discovery and development milestones, our future discovery and development efforts, including regulatory submissions and approvals, our commercialization efforts, our partnerships and collaborations with third parties, our future operating results and financial position, our business strategy, and other objectives for future operations. We often use words such as "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and other words and terms of similar meaning to help identify forward-looking statements, although not all forward-looking statements contain these identifying words. You also can identify these forward-looking statements by the fact that they do not relate strictly to historical or current facts. There are a number of important risks and uncertainties that could cause actual results or events to differ materially from those indicated by forward-looking statements. These risks and uncertainties include, but are not limited to, those described in Part II, Item 1A - Risk Factors of this Quarterly Report on Form 10-Q. As a result of these and other factors, we may not actually achieve the plans, intentions, expectations or results disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

References to XPOVIO® (selinexor) also refer to NEXPOVIO® (selinexor) when discussing its approval and commercialization in certain countries or territories outside of the U.S.

**OVERVIEW**

We are a commercial-stage pharmaceutical company pioneering novel cancer therapies and dedicated to the discovery, development and commercialization of first-in-class drugs directed against nuclear export for the treatment of cancer and other diseases. Our scientific expertise is based upon an understanding of the regulation of intracellular communication between the nucleus and the cytoplasm. We have discovered and are developing and commercializing novel, small molecule **S**elective **I**nhibitor of **N**uclear **E**xport ("SINE") compounds that inhibit the nuclear export protein exportin 1 ("XPO1"). These SINE compounds represent a new class of drug candidates with a novel mechanism of action that have the potential to treat a variety of diseases with high unmet medical need. Our lead asset, XPOVIO® (selinexor), was the first oral XPO1 inhibitor to receive marketing approval, receiving its initial U.S. approval from the U.S. Food and Drug Administration ("FDA") in July 2019, and is currently approved and marketed in the U.S. for the following indications:

- In combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy. Approval in this indication was based on the results from the BOSTON (**Bo**rtezomib, **S**elinexor and Dexame**t**has**on**e) trial;
- In combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody. Approval in this indication was based on the results from the STORM (**S**elinexor **T**reatment of **R**efractory **M**yeloma) trial; and
- For the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma ("DLBCL"), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least two lines of systemic therapy. This indication was approved under accelerated approval based on response rate and was based on the results from the SADAL (**S**elinexor **A**gainst **D**iffuse **A**ggressive **L**ymphoma) trial. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

The commercialization of XPOVIO in the U.S. is currently supported by sales representatives, nurse liaisons, and a market access team, as well as KaryForward™, an extensive patient and healthcare provider support program. Our commercial efforts are also

supplemented by patient support initiatives coordinated by our dedicated network of participating specialty pharmacy providers. We plan to continue to educate physicians, other healthcare providers and patients about XPOVIO's clinical profile and unique mechanism of action as we continue to expand XPOVIO use.

The commercialization of XPOVIO and NEXPOVIO® (selinexor) (the brand name for selinexor in Europe and the United Kingdom) outside of the U.S. is managed by our partners in their respective territories. XPOVIO/NEXPOVIO has received regulatory approval in various indications in over 40 countries outside the U.S. and is commercially available in a growing number of countries as our partners continue to secure reimbursement approvals.

Our primary focus is on marketing XPOVIO in its currently approved indications as well as developing and seeking the regulatory approval of selinexor as an oral agent targeting multiple high unmet need cancer indications, including our core programs in endometrial cancer, multiple myeloma, and myelofibrosis. We plan to continue to conduct clinical trials and to seek additional approvals for the use of selinexor as a single agent or in combination with other oncology therapies to expand the patient populations that are eligible for treatment with selinexor. In January 2024, we announced that further clinical development of our eltanexor program is on hold in an effort to focus our resources on our prioritized late-stage programs.

As of March 31, 2024, we had an accumulated deficit of $1.5 billion. We had net losses of $37.4 million and $34.1 million for the three months ended March 31, 2024 and 2023, respectively.

In May 2024, we entered into a series of transactions to limit our aggregate indebtedness, extend the maturity of certain of our indebtedness and provide us with additional working capital. Pursuant to these transactions, we borrowed $100.0 million from existing lenders and certain entities managed by HealthCare Royalty Management, LLC ("HCRx") under a new, senior secured term loan facility and used a portion of the proceeds of that loan to repay obligations under our existing financing arrangement with HCRx pursuant to an amendment that made other changes to our existing financing arrangement with HCRx. We also entered into privately negotiated agreements to exchange $148.0 million aggregate principal amount of our existing unsecured convertible senior notes for (i) $111.0 million aggregate principal amount of our new secured convertible senior notes and (ii) warrants to purchase up to 46.0 million shares of our common stock. In addition, HCRx agreed to purchase $5.0 million aggregate principal amount of our new secured convertible senior notes through satisfaction of $5.0 million of our existing obligations to HCRx. Please refer to Note 10 "*Long-Term Obligations*", to the condensed consolidated financial statements contained within Part I, Item 1 of this Quarterly Report on Form 10-Q for additional details of these refinancing transactions.

**CRITICAL ACCOUNTING ESTIMATES**

We believe that several accounting policies are important to understanding our historical and future performance. We refer to these policies as "critical" because these specific areas generally require us to make judgments and estimates about matters that are uncertain at the time we make the estimate, and different estimates - which also would have been reasonable - could have been used, which would have resulted in different financial results.

There have been no changes to the critical accounting estimates we identified in Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations in our Annual Report.

**RESULTS OF OPERATIONS**

The following table summarizes our results of operations (in thousands, except for percentages):

| | For the Three Months Ended March 31, | | | |
|---|---|---|---|---|
| | 2024 | 2023 | $ Change | % Change |
| Product revenue, net | $ 26,006 | $ 28,288 | $ (2,282) | (8)% |
| License and other revenue | 7,120 | 10,410 | (3,290) | (32)% |
| Total revenue | 33,126 | 38,698 | (5,572) | (14)% |
| Operating expenses: | | | | |
| Cost of sales | 1,911 | 1,351 | 560 | 41% |
| Research and development | 35,425 | 32,339 | 3,086 | 10% |
| Selling, general and administrative | 29,549 | 35,907 | (6,358) | (18)% |
| Loss from operations | (33,759) | (30,899) | (2,860) | 9% |
| Other expense, net | (3,532) | (3,173) | (359) | 11% |
| Loss before income taxes | (37,291) | (34,072) | (3,219) | 9% |
| Income tax provision | (71) | (54) | (17) | 31% |
| Net loss | $ (37,362) | $ (34,126) | $ (3,236) | 9% |

***Product Revenue, net (in thousands, except for percentages)***

| | For the Three Months Ended March 31, | | | |
|---|---|---|---|---|
| | 2024 | 2023 | $ Change | % Change |
| Product revenue, net | $ 26,006 | $ 28,288 | $ (2,282) | (8)% |

To date, our only source of product revenue has been from the U.S. sales of XPOVIO. Net product revenue for the three months ended March 31, 2024 decreased as compared to the three months ended March 31, 2023, primarily due to decreased demand as a result of increasing competition and higher gross-to-net driven by increased Medicare/Medicaid rebates and 340B discounts.

We expect product revenue to increase slightly in the second quarter of 2024 as compared to the first quarter of 2024 driven largely by gross-to-net favorability.

***License and Other Revenue (in thousands, except for percentages)***

| | For the Three Months Ended March 31, | | | |
|---|---|---|---|---|
| | 2024 | 2023 | $ Change | % Change |
| Menarini Group ("Menarini") | $ 6,406 | $ 8,737 | $ (2,331) | (27)% |
| Antengene Therapeutics Limited ("Antengene") | 511 | 1,112 | (601) | (54)% |
| Other | 203 | 561 | (358) | (64)% |
| Total license and other revenue | $ 7,120 | $ 10,410 | $ (3,290) | (32)% |

License and other revenue for the three months ended March 31, 2024 decreased by $3.3 million as compared to the three months ended March 31, 2023 primarily due to $3.5 million of non-recurring license-related revenue recognized from Menarini during the three months ended March 31, 2023, partially offset by a $1.0 million increase in revenue for the reimbursement of development-related expenses from Menarini due to a corresponding increase in the underlying expenses during the three months ended March 31, 2024.

We expect license and other revenue to increase in the second quarter of 2024 as compared to the first quarter of 2024 due to milestone achievements and increased royalties expected from our partners.

***Operating Expenses (in thousands, except for percentages)***

| | For the Three Months Ended March 31, | | | |
|---|---|---|---|---|
| | 2024 | 2023 | $ Change | % Change |
| Cost of sales | $ 1,911 | $ 1,351 | $ 560 | 41% |
| Research and development | 35,425 | 32,339 | 3,086 | 10% |
| Selling, general and administrative | 29,549 | 35,907 | (6,358) | (18)% |
| Total operating expenses | $ 66,885 | $ 69,597 | $ (2,712) | (4)% |

***Cost of Sales***

Cost of sales were consistent for the three months ended March 31, 2024 and 2023. We expect cost of sales to continue to remain relatively consistent in the second quarter of 2024 as compared to the first quarter of 2024.

***Research and Development Expenses (in thousands, except for percentages)***

| | For the Three Months Ended March 31, | | | |
|---|---|---|---|---|
| | 2024 | 2023 | $ Change | % Change |
| Clinical trial and related costs: | | | | |
| Selinexor in myelofibrosis | $ 6,382 | $ 985 | $ 5,397 | 548% |
| Selinexor in endometrial cancer | 4,407 | 3,418 | 989 | 29% |
| Selinexor in multiple myeloma | 4,037 | 1,431 | 2,606 | 182% |
| Other programs | 435 | 3,762 | (3,327) | (88)% |
| Non-program specific clinical trial and related costs | 2,119 | 2,445 | (326) | (13)% |
| Total clinical trial and related costs | 17,380 | 12,041 | 5,339 | 44% |
| Unallocated costs: | | | | |
| Personnel | 11,888 | 14,173 | (2,285) | (16)% |
| Consulting, professional and other | 4,736 | 4,187 | 549 | 13% |
| Stock-based compensation | 1,421 | 1,938 | (517) | (27)% |
| Total unallocated costs | 18,045 | 20,298 | (2,253) | (11)% |
| Total research and development expenses | $ 35,425 | $ 32,339 | $ 3,086 | 10% |

At any one time, we have a number of ongoing clinical development programs that we are conducting independently or in collaboration with third parties. We track our external clinical trial and related costs on a program-by-program basis. Our major programs include our three core clinical development programs in myelofibrosis, multiple myeloma and endometrial cancer. To the extent that external clinical trial and related costs are not attributable to a major program, they are included in "*Other programs*" and to the extent external clinical trial and related costs cannot be allocated to a specific program, they are included in "*Non-program specific clinical trial and related costs*." We also have unallocated research and development costs, which we do not track on a program-by-program basis. These costs represent costs that are incurred across multiple programs or to support our general research and development operations.

Research and development expenses for the three months ended March 31, 2024 increased by $3.1 million as compared to the three months ended March 31, 2023. The $5.3 million increase in clinical trial and related costs was primarily due to increased activity in each of our three ongoing pivotal Phase 3 trials, including increased purchases of comparator drugs. These increases were partially offset by decreases of clinical trial and related costs in other programs, primarily KPT-1200, our IL-12 product that we sold to Libo Pharma Corp. in December 2023, and eltanexor.

The decrease in personnel costs of $2.3 million was primarily due to a reduction in headcount and contractors for the three months ended March 31, 2024 as compared to the three months ended March 31, 2023.

We expect our research and development expenses to increase slightly in the second quarter of 2024 as compared to the first quarter of 2024 as we continue to progress our three pivotal Phase 3 trials.

***Selling, General and Administrative Expenses (in thousands, except for percentages)***

| | For the Three Months Ended March 31, | | | |
|---|---|---|---|---|
| | 2024 | 2023 | $ Change | % Change |
| Personnel costs | $ 15,967 | $ 18,821 | $ (2,854) | (15)% |
| Consulting, professional and other costs | 10,087 | 13,716 | (3,629) | (26)% |
| Stock-based compensation | 3,495 | 3,370 | 125 | 4% |
| Total selling, general and administrative expenses | $ 29,549 | $ 35,907 | $ (6,358) | (18)% |

Selling, general and administrative expenses for the three months ended March 31, 2024 decreased by $6.4 million as compared to the three months ended March 31, 2023. The decrease in personnel costs of $2.9 million was primarily due to a reduction in headcount and contractors. The $3.6 million decrease in consulting, professional and other costs was primarily due to our ongoing cost reduction initiatives.

We expect our selling, general and administrative expenses to remain relatively consistent in the second quarter of 2024 as compared to the first quarter of 2024.

***Other Expense, net (in thousands, except for percentages)***

| | For the Three Months Ended March 31, | | | |
|---|---|---|---|---|
| | 2024 | 2023 | $ Change | % Change |
| Interest expense | $ (5,884) | $ (5,758) | $ (126) | 2% |
| Interest income | 2,156 | 2,849 | (693) | (24)% |
| Other income (expense) | 196 | (264) | 460 | (174)% |
| Total other expense, net | $ (3,532) | $ (3,173) | $ (359) | 11% |

Other expense, net for the three months ended March 31, 2024 increased by $0.4 million, as compared to the three months ended March 31, 2023, primarily due to a $0.7 million decrease in interest income resulting from lower investment balances during the three months ended March 31, 2024.

We expect other expense, net to increase slightly in the second quarter of 2024 as compared to the first quarter of 2024, due to the interest payments on the new term loan and new secured convertible senior notes, offset by a decrease in payments to HCRx.

## LIQUIDITY AND CAPITAL RESOURCES

### Cash Flows

To date, we have financed our operations primarily through a combination of product revenue sales, private placements of our common stock, proceeds from public offerings of our common stock, proceeds from the issuance of convertible debt, proceeds pursuant to the deferred royalty obligation, proceeds from a term loan, and cash generated from our business development activities. As of March 31, 2024, our principal source of liquidity was $148.6 million of cash, cash equivalents and investments. We have had recurring losses since inception and incurred a loss of $37.4 million for the three months ended March 31, 2024. We expect that our cash, cash equivalents and investments at March 31, 2024 will be sufficient to fund our current operating plans and capital expenditure requirements for at least twelve months from the date of issuance of the financial statements contained in this Quarterly Report on Form 10-Q.

The following table provides information regarding our cash flows (in thousands):

| | For the Three Months Ended March 31, | | | |
|---|---|---|---|---|
| | 2024 | 2023 | $ Change | % Change |
| Net cash used in operating activities | $ (43,725) | $ (18,910) | $ (24,815) | 131% |
| Net cash provided by (used in) investing activities | 21,940 | (32,388) | 54,328 | (168)% |
| Effect of foreign exchange rates | (16) | (45) | 29 | (64)% |
| Net decrease in cash, cash equivalents and restricted cash | $ (21,801) | $ (51,343) | $ 29,542 | (58)% |

*Operating activities.* The $24.8 million increase in net cash used in operating activities for the three months ended March 31, 2024 compared to the three months ended March 31, 2023 was primarily driven by the collection of $22.4 million of milestone payments from Antengene in the first quarter of 2023.

*Investing activities.* The $54.3 million decrease in net cash used in investing activities for the three months ended March 31, 2024 compared to the three months ended March 31, 2023 was driven by a $25.8 million increase in proceeds from the sales and maturities of investments and a $28.7 million decrease in purchases of investments.

**Sources of Liquidity**

On September 14, 2019, we and certain of our subsidiaries entered into the Revenue Interest Financing Agreement with HealthCare Royalty Partners III, L.P. and HealthCare Royalty Partners IV, L.P. ("HCRx"), which was subsequently amended on June 23, 2021, August 1, 2023 and May 2024 (the "Revenue Interest Agreement" and, as amended, the "Amended Revenue Interest Agreement").

Pursuant to the Revenue Interest Agreement, HCRx paid us $75.0 million, less certain transaction expenses, on September 27, 2019, and pursuant to the Amended Revenue Interest Agreement, HCRx paid us $60.0 million, less certain transaction expenses, on June 23, 2021. For additional information on the Amended Revenue Interest Agreement, see Note 10, "*Long-Term Obligations*", to the condensed consolidated financial statements included under Part I, Item I of this Quarterly Report on Form 10-Q.

On February 17, 2023, we entered into an Open Market Sale Agreement (the "2023 Open Market Sale Agreement") with Jefferies LLC, as agent ("Jefferies"). Under the 2023 Open Market Sale Agreement, we may issue and sell shares of our common stock having an aggregate offering price of up to $100.0 million (the "Shares") from time to time through Jefferies. We did not sell any Shares under the 2023 Open Market Sales Agreement during the three months ended March 31, 2024 and 2023. As of March 31, 2024, $100.0 million of Shares was available for issuance and sale under the 2023 Open Market Sale Agreement.

During the three months ended March 31, 2024, we received $7.1 million in milestone and upfront payments under our license and distribution agreements pursuant to which we are entitled to receive additional milestone payments, if certain development goals and sales milestones are achieved as well as royalties on future net sales of the licensed and sold products in the territories under such arrangements. In addition, under the license agreement we entered into with Menarini in December 2021 (the "Menarini Agreement"), Menarini will reimburse us for 25% of all documented expenses we incur for the global development of selinexor from 2022 through 2025, provided that such reimbursements shall not exceed $15.0 million per calendar year. We did not receive any reimbursements under the Menarini Agreement during the three months ended March 31, 2024.

**Commitments, Contingencies and Contractual Obligations**

***Operating Leases***

We are party to an operating lease of 98,502 square feet of office and research space in Newton, Massachusetts with a term through September 30, 2025 (the "Newton, MA Lease"). Pursuant to the Newton, MA Lease, we have provided a security deposit in the form of a cash-collateralized letter of credit in the amount of $0.3 million which is classified in long-term restricted cash on our condensed consolidated balance sheets. We expect to incur total lease costs of $5.8 million from March 31, 2024 to September 30, 2025.

In addition, we are party to certain short-term leases having a term of twelve months or less at the commencement date. We recognize short-term lease expense on a straight-line basis and do not record a related right-of-use asset or lease liability for such leases. These costs were insignificant for both the three months ended March 31, 2024 and 2023.

***Contractual Obligations***

We have contractual obligations under our 3.00% Convertible Senior Notes due 2025 (the "Notes") and under our Amended Revenue Interest Agreement as disclosed in Note 10, "*Long-Term Obligations*", to the condensed consolidated financial statements included under Part I, Item 1 of this Quarterly Report on Form 10-Q.

**Funding Requirements**

We expect to continue to incur costs related to our clinical development programs as we rapidly advance three pivotal Phase 3 trials, as well as commercialization expenses related to sales, marketing, manufacturing and distribution of our approved products, to the extent that these functions are not the responsibility of our collaborators.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete. In addition, our product candidates for which we receive marketing approval may not achieve commercial success. Our ability to become and remain profitable depends on our ability to generate revenue. There can be no assurance as to the amount or timing of any such revenue, and we may not achieve profitability for several years, if at all, as described

more fully in the risk factor entitled "*We have incurred significant losses since inception, expect to continue to incur significant losses, and may never achieve or maintain profitability*," under the heading "*Risk Factors*" in this Quarterly Report on Form 10-Q. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. We may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or commercialization efforts.

We currently expect that cash, cash equivalents and investments at March 31, 2024 will be sufficient to fund our current operating plans and capital expenditure requirements for at least twelve months from the date of issuance of the financial statements contained in this Quarterly Report on Form 10-Q while we continue to commercialize XPOVIO in the U.S. and continue the clinical trials of our product candidates. Our future long-term capital requirements will depend on many factors, as described more fully in the risk factor entitled "*We will need additional funding to achieve our business objectives. If we are unable to raise capital when needed or on acceptable terms, we would be forced to delay, reduce or eliminate our research and development programs and/or commercialization efforts*," under the heading *"Risk Factors*" in this Quarterly Report on Form 10-Q.

In addition to the expenses required to fund our operations described above, our funding requirements as of March 31, 2024 also include the following:

- Lease costs for our headquarters in Newton, Massachusetts with a term through September 30, 2025. We expect to incur total lease costs of $5.8 million from March 31, 2024 to September 30, 2025;
- Future long-term debt obligations related to the 2025 Notes of $182.9 million over the next two years; and
- Future royalty obligations to HCRx under the Amended Revenue Interest Agreement of $197.5 million.

Please refer to Note 10 "*Long-Term Obligations*", to the condensed consolidated financial statements contained within Part I, Item 1 of this Quarterly Report on Form 10-Q for a summary of the refinancing transactions we entered into subsequent to March 31, 2024 which affect the above funding requirements.

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

We are exposed to market risk related to changes in interest rates. We had cash, cash equivalents and investments of $148.6 million as of March 31, 2024. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 100 basis point shift in interest rates would not have a material effect on the fair market value of our investment portfolio.

We do not believe our cash, cash equivalents and investments have significant risk of default or illiquidity. While we believe our cash, cash equivalents and investments do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in securities at one or more financial institutions that are in excess of federally insured limits. Given the potential instability of financial institutions, we cannot provide assurance that we will not experience losses on these deposits and investments.

We are also exposed to market risk related to changes in foreign currency exchange rates. We contract with contract research organizations and contract manufacturing organizations that are located in Canada, the United Kingdom and Europe, which are denominated in foreign currencies. We also contract with a number of clinical trial sites outside of the U.S., and our budgets for those studies are frequently denominated in foreign currencies. We are subject to fluctuations in foreign currency rates in connection with these agreements. We do not currently hedge our foreign currency exchange rate risk.

**Item 4. Controls and Procedures.**

**Evaluation of Disclosure Controls and Procedures**

Our management, with the participation of our President and Chief Executive Officer (principal executive officer) and Executive Vice President, Chief Financial Officer and Treasurer (principal financial officer), evaluated the effectiveness of our disclosure controls and procedures as of March 31, 2024. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the “Exchange Act”), means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to our management, including our principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies our judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of March 31, 2024, our President and Chief Executive Officer and our Executive Vice President, Chief Financial Officer and Treasurer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

**Changes in Internal Control Over Financial Reporting**

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the fiscal quarter ended March 31, 2024 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

## PART II - OTHER INFORMATION

### Item 1A. Risk Factors.

*Careful consideration should be given to the following material risk factors, in addition to the other information set forth in this Quarterly Report on Form 10-Q and in other documents that we file with the U.S. Securities and Exchange Commission ("SEC") in evaluating us and our business. Investing in our common stock involves a high degree of risk. If any of the following risks and uncertainties actually occurs, our business, prospects, financial condition and results of operations could be materially and adversely affected. The risks described below are not intended to be exhaustive and are not the only risks we face. New risk factors can emerge from time to time, and it is not possible to predict the impact that any factor or combination of factors may have on our business, prospects, financial condition and results of operations.*

*References to XPOVIO® (selinexor) also refer to NEXPOVIO® (selinexor) when discussing its approval and commercialization in certain countries or territories outside of the U.S.*

#### Risks Related to Commercialization and Product Development

***Our business is substantially dependent on the commercial success of XPOVIO. If we, either alone or with our collaborators, are unable to successfully commercialize current and future indications of XPOVIO or other products or product candidates on a timely basis, including achieving widespread market acceptance by physicians, patients, third-party payors and others in the medical community, our business, financial condition and future profitability will be materially harmed.***

Our business and our ability to generate product revenue from the sales of drugs that treat cancer depend heavily on our and our collaborators' ability to successfully commercialize our lead drug, XPOVIO® (selinexor), on a global basis in currently approved and future indications, and the level of market adoption for, and the continued use of, our products and product candidates, if approved. XPOVIO is currently approved and marketed in the U.S. in multiple hematologic malignancy indications, including in combination with bortezomib and dexamethasone for the treatment of patients with multiple myeloma who have received at least one prior therapy, in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody; and as a monotherapy for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma ("DLBCL"), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy. Efforts to drive adoption within the medical community and third-party payors based on the benefits of our products and product candidates require significant resources and may not be successful. The success of XPOVIO and any current or future product candidates, whether alone or in collaboration with third parties, including achieving and maintaining an adequate level of market adoption, depends on several factors, including:

- our ability to achieve broad adoption of XPOVIO in earlier lines of therapy or to successfully launch and achieve broad adoption of any future XPOVIO indications or any product candidates for which we obtain marketing approval;
- the competitive landscape for our products, including the timing of new competing products entering the market and the level and speed at which these products achieve market acceptance;
- actual or perceived advantages or disadvantages of our products or product candidates as compared to alternative treatments, including their respective safety, tolerability and efficacy profiles, the potential convenience and ease of administration, access or cost effectiveness;
- the effectiveness of our sales, marketing, manufacturing and distribution strategies and operations;
- the consistency of any new data we collect and analyses we conduct with prior results, whether they support a favorable safety, efficacy and effectiveness profile of XPOVIO and any potential impact on our U.S. Food and Drug Administration ("FDA") approvals and/or FDA package insert for XPOVIO and comparable foreign regulatory approvals and package inserts;
- our ability to comply with the FDA's and comparable foreign regulatory authorities' post-marketing requirements and commitments, including through successfully conducting, on a timely basis, additional studies that confirm clinical efficacy, effectiveness and safety of XPOVIO and acceptance of the same by the FDA or similar foreign regulatory bodies;
- acceptance of current indications of XPOVIO and future indications of XPOVIO and other product candidates, if approved, by patients, the medical community and third-party payors;
- obtaining and maintaining coverage, adequate pricing and reimbursement by third-party payors, including government payors, for XPOVIO and our product candidates, if approved;

- the willingness of patients to pay out-of-pocket in the absence of third-party coverage or as co-pay amounts under third-party coverage; for example, multiple myeloma foundation closures during 2023 resulted in significantly increased use of our Patient Assistance Program ("PAP"), which adversely impacted our 2023 revenues;
- our ability to enforce intellectual property rights in and to our products to prohibit a third-party from marketing a competing product and our ability to avoid third-party patent interference or intellectual property infringement claims;
- current and future restrictions or limitations on our approved or future indications and patient populations or other adverse regulatory actions;
- the performance of our manufacturers, license partners, distributors, providers and other business partners, over which we have limited control;
- any significant misestimations of the size of the market and market potential for any of our products or product candidates;
- establishing and maintaining commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies, based, in part, on their perception of our clinical trial data and/or the actual or perceived safety, tolerability and effectiveness profile;
- maintaining an acceptable safety and tolerability profile of our approved products, including the prevalence and severity of any side effects;
- the ability to offer our products for sale at competitive prices;
- adverse publicity about our products or favorable publicity about competitive products;
- our ability to maintain compliance with existing and new health care laws and regulations, including government pricing, price reporting and other disclosure requirements related to such laws and regulations, and the potential impact of such laws and regulations on physician prescribing practices and payor coverage; and
- the ability of our sales force to meet with healthcare professionals in person.

If we do not achieve one or more of these factors in a timely manner, or at all, either on our own or with our collaborators, we could experience significant delays or an inability to successfully commercialize XPOVIO or our product candidates, if approved, which would materially harm our business.

***We face substantial competition, which may result in others discovering, developing or commercializing drugs before or more successfully than we do.***

The discovery, development and commercialization of new drugs is highly competitive, particularly in the cancer field. We and our collaborators face competition with respect to XPOVIO and will face competition with respect to any product candidates that we may seek to discover and develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, academic institutions and governmental agencies as well as public and private research institutions worldwide, many of which have significantly greater financial resources and expertise in research and development, manufacturing, preclinical studies, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. There are a number of major pharmaceutical, specialty pharmaceutical and biotechnology companies that currently market and sell drugs and/or are pursuing the development of drugs for the treatment of cancer and the other disease indications for which we, and our collaborators, are developing our product candidates. Several new novel therapeutics have recently entered, and are expected to continue to enter, the multiple myeloma treatment landscape. For example, TECVAYLI™ (teclistamab-cqyv), the first bispecific T-Cell engager, was approved by the FDA in October 2022, followed by approvals of two more bispecifics, ELREXFIO™ (elranatamab-bcmm) and TALVEY™ (talquetamab-tgvs) in August 2023. Other T-cell engaging therapies, bispecifics with different targets, and immunomodulators are in clinical development and may be introduced into the multiple myeloma market in 2024 and beyond. CARVYKTI® (ciltacabtagene autoleucel; cilta-cel) and Abecma® (idecabtagene vicleucel; ide-cel) were approved in April 2024 for the treatment of multiple myeloma in earlier lines. In addition, future label expansions into earlier lines of existing therapies are anticipated in 2024 and beyond. The approval of these anti-cancer agents, or any others which may receive regulatory approval, have had a significant impact and may continue to have a significant impact on the therapeutic landscape and our product revenues. See Item 1 under the heading *Business - Competition* in our Annual Report on Form 10-K for the year ended December 31, 2023 as filed with the SEC on February 29, 2024 for more information on competition.

We are currently focused on developing and commercializing our products and product candidates for the treatment of cancer and there are a variety of available therapies marketed for cancer. In many cases, cancer drugs are administered in combination to enhance efficacy. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well-established therapies and are widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic drugs. Our products are priced at a significant premium over competitive generic drugs, which may make it difficult for us to achieve our business strategy of using our products in combination with existing therapies or replacing existing therapies with our products.

Further, our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are or are perceived to be more effective, safer, more tolerable, more convenient and/or less costly than any of our currently approved products or product candidates or that would render our products obsolete or non-competitive. Our competitors may also obtain marketing approval from the FDA or other regulatory authorities for their products more rapidly than we, or our collaborators, may obtain approval for ours, which could result in our competitors establishing a stronger market position before we, or our collaborators, are able to enter the market or preventing us, or our collaborators, from entering into a particular indication at all.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or that may be necessary for, our programs.

If we are not able to compete effectively against current or potential competitors, our business will not grow and our financial condition and operations will suffer.

***Clinical development is a lengthy and expensive process, with uncertain timelines and outcomes. We or our collaborators may be unable to successfully enroll patients in our ongoing and planned clinical trials in a reasonable timeframe, or at all. In addition, if clinical trials of our product candidates fail to demonstrate safety and effectiveness to the satisfaction of regulatory authorities or do not otherwise produce positive results, we, or our collaborators, may incur additional costs, fail to secure regulatory approvals, or be unable to commercialize such product candidates.***

Our long-term success depends in a large part on our ability to continue to successfully develop new indications of selinexor, our product candidates, or any new product candidates we may develop or acquire. Clinical testing is expensive, time consuming, difficult to design, implement and enroll, inherently uncertain as to outcome and can fail at any stage of testing. Furthermore, the failure of any product candidates to demonstrate safety and effectiveness in any clinical trial could negatively impact the perception of selinexor or our other product candidates and/or cause the FDA or other regulatory authorities to require additional testing before any of our product candidates are approved.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our or our collaborators' ability to complete such clinical trials or receive marketing approval of our product candidates, including, but not limited to, the following:

- delays or failure to reach agreement with regulatory authorities on a trial design or the receipt of feedback requiring us to modify the design of our clinical trials, perform additional or unanticipated clinical trials to obtain approval or alter our regulatory strategy, as is the case in connection with the feedback we received from the FDA in February 2022 on our SIENDO Study;
- clinical trials of our product candidates may produce negative or inconclusive results or other patient safety concerns, including undesirable side effects or other unexpected characteristics, and we may decide, or regulatory authorities may require us, to conduct additional clinical trials, suspend ongoing clinical trials or abandon drug development programs, including as a result of a finding that the participants are being exposed to unacceptable health risks;
- enrollment in our clinical trials may be slower than we anticipate, including as a result of competition with other ongoing clinical trials, delays in site activation, newly approved competitive products for the same indications as our product candidates or new or amended regulations; for example, in 2023, site activation for our Phase 3 clinical trial in endometrial cancer was delayed in the EU due to the recent adoption of the In Vitro Diagnostic Devices Regulation, as discussed further below;
- regulators may revise the requirements for approving our product candidates, even after providing a positive opinion on or otherwise reviewing and providing comments to a clinical trial protocol, and/or such requirements may not be as we anticipate;

- delays or failure in obtaining the necessary authorization from regulatory authorities or institutional review boards to permit us, our collaborators or our investigators to commence a clinical trial, conduct a clinical trial at a prospective trial site, or the suspension or termination of a clinical trial once commenced. For example, the continuation of a clinical trial in Europe with the transition to the EU Clinical Trials Regulation ("CTR") now requires submission of ongoing and new clinical trials conducted in Europe to the Clinical Trial Information System;
- delays or failure to reach agreement on acceptable terms with prospective clinical trial sites or contract research organizations ("CROs");
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors, including manufacturers or CROs, may fail to comply with regulatory requirements, perform effectively, or meet their contractual obligations to us in a timely manner, or at all;
- we or our investigators might be found to be non-compliant with regulatory requirements;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials may be insufficient or inadequate;
- for any biomarker driven clinical trial, the potential regulatory requirement to utilize a companion diagnostic, for example the required use of a companion diagnostic for our ongoing study evaluating selinexor in patients with *TP53* wild-type advanced or recurrent endometrial cancer;
- any partners or collaborators that help us conduct clinical trials may face any of the above issues, and may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us; and
- negative impacts resulting from a pandemic or other public health emergency, including impacts to healthcare systems and our trial sites' ability to conduct trial.

If we, or our collaborators, are required to conduct additional clinical trials or other testing of our product candidates or a companion diagnostic beyond those that we currently contemplate or are unable to successfully complete clinical trials of our product candidates or other testing, on a timely basis or at all, and/or if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we, or our collaborators, may:

- be delayed in obtaining, or not obtain at all, marketing approval for the indication or product candidate;
- obtain marketing approval in some countries and not in others;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements;
- not receive royalty or milestone revenue under our collaboration agreements for several years, or at all; or
- have the product removed from the market after obtaining marketing approval.

Further, we do not know whether clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. In addition, if we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted. For example, in December 2022, with the passage of Food and Drug Omnibus Reform Act ("FDORA"), Congress required sponsors to develop and submit a diversity action plan for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Similarly, the regulatory landscape related to clinical trials in the EU recently evolved. The CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application to be submitted in each member state, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. If we are not able to fulfill these new requirements, our ability to conduct clinical trials may be delayed or halted.

Any of these events could prevent us or our collaborators from achieving or maintaining market acceptance of the affected product candidate, if approved, or could substantially increase costs and expenses of development or commercialization, which could

delay or prevent us from generating sufficient revenue from the sale of our products and harm our business and results of operations. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our products, allow our competitors to bring products to market before we do or impair our ability to successfully commercialize our products, which would harm our business and results of operations. In addition, many of the factors that cause, or lead to, clinical trial delays may ultimately lead to the denial of regulatory approval of our product candidates.

***Serious adverse or unacceptable side effects related to XPOVIO, our product candidates or future products may delay or prevent their regulatory approval, cause us or our collaborators to suspend or discontinue clinical trials, limit the commercial value of approved indications or result in significant negative financial consequences following any marketing approval.***

We are currently developing selinexor for the treatment of multiple types of cancer. Its risk of failure is high. If our current or future indications of XPOVIO, any of our product candidates or future products are associated with undesirable side effects or have characteristics that are unexpected in clinical trials or following approval and/or commercialization, we may need to abandon or limit their development or limit marketing to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective.

Adverse events ("AEs") in our clinical trials for selinexor to date have been generally predictable and typically manageable, including through prophylactic care or dose reductions, although some patients have experienced more serious AEs. The most common drug-related AEs in our clinical trials for selinexor include fatigue, nausea, anorexia, diarrhea, peripheral neuropathy, upper respiratory tract infection, vomiting, cytopenias, hyponatremia, weight loss, decreased appetite, cataract, dizziness, syncope, depressed level of consciousness, and mental status changes. These side effects were generally mild or moderate in severity. The most common AEs that are Grade 3 or Grade 4, meaning they are more than mild or moderate in severity, include thrombocytopenia, lymphopenia, hypophosphatemia, anemia, hyponatremia and neutropenia. To date, the most common AEs in the multiple myeloma patient population have been managed with supportive care and dose modifications. However, a number of patients have withdrawn from our clinical trials as a result of AEs and some patients across our clinical trials have experienced serious AEs deemed by us and the clinical investigator to be related to selinexor. Serious AEs generally refer to AEs that result in death, are life threatening, require hospitalization or prolonging of hospitalization, or cause a significant and permanent disruption of normal life functions, congenital anomalies or birth defects, or require intervention to prevent such an outcome.

The occurrence of AEs in either our clinical trials or following regulatory approval could result in a more restrictive label for any product candidates approved for marketing or could result in the delay or denial of approval to market any product candidates by the FDA or comparable foreign regulatory authorities, which could prevent us from generating sufficient revenue from product sales or ultimately achieving profitability. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial, result in potential product liability claims or cause patients and/or healthcare providers to elect alternative courses of treatment. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. Inadequate training or education of healthcare professionals to recognize or manage the potential side effects of XPOVIO or our product candidates, if approved, could result in increased treatment-related side effects and cause patients to discontinue treatment. Any of these occurrences may harm our business, financial condition and prospects significantly.

Results of our trials could reveal an unacceptably high severity and prevalence of side effects. In such an event, our trials could be suspended or terminated by us or the FDA or comparable foreign regulatory authorities could order us or our collaborators to cease further development of or deny approval of our product candidates for any or all targeted indications. Many compounds that initially showed promise in early-stage trials for treating cancer or other diseases have later been found to cause side effects that prevented further development of the compound. If such an event occurs after any of our or our collaborators' product candidates are approved and/or commercialized, a number of potentially significant negative consequences may result, including:

- regulatory authorities may withdraw the approval of such drug, require additional warnings on the label or impose distribution or use restrictions and/or require one or more post-marketing studies;
- patients and/or healthcare providers may elect to utilize other treatment options that have or are perceived to have more tolerable side effects;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Further, we, our collaborators and our clinical trial investigators, currently determine if serious adverse or unacceptable side effects are drug-related. The FDA or foreign regulatory authorities may disagree with our, our collaborators' or our clinical trial investigators' interpretation of data from clinical trials and the conclusion by us, our collaborators or our clinical trial investigators that

a serious adverse effect or unacceptable side effect was not drug-related. The FDA or foreign regulatory authorities may require more information related to the safety of our products or product candidates, including additional preclinical or clinical data to support approval, which may cause us to incur additional expenses, delay or prevent the approval of one of our product candidates, and/or delay or cause us to change our commercialization plans, or we may decide to abandon the development of the product candidate altogether.

***The results of previous clinical trials may not be predictive of future trial results, and interim or top-line data may be subject to change or qualification based on the complete analyses of data and, therefore, may not be predictive of the final results of a trial.***

Clinical failure can occur at any stage of the clinical development process and, therefore, the outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later stage clinical trials. Finalization and cleaning of data from our clinical trials may change the conclusions drawn from uncleaned data provided by our clinical trial investigators. Further, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, starting dose, adherence to the dosing regimen and other trial protocols and the dropout rate among clinical trial participants. We do not know whether any Phase 2, Phase 3 or other clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety data sufficient to obtain regulatory approval to market our product candidates, if approved. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we could face similar setbacks.

We may publicly disclose preliminary, interim or top-line data from our clinical trials. These interim updates are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change as further patient data become available and following a more comprehensive review of the data related to the particular study or trial. For example, on February 8, 2022, we announced positive top-line data results for the SIENDO Study. On February 25, 2022, we discussed these data with the FDA in a pre-sNDA meeting. We and the FDA meeting participants had differing views on the statistical significance of the study and the overall clinical benefit for the whole study population. For this study or any other study for which we report preliminary, interim or top-line data, we make assumptions, estimations, calculations and conclusions as part of our analyses of data. We may not have received or had the opportunity to fully and carefully evaluate all data or perform all analyses or our conclusions may differ from those of the FDA or other regulatory authorities. Consequently, the interpretation of preliminary, interim or top-line data results that we report may differ from future interpretations of the same studies once additional data have been received and fully evaluated or based on differing views from regulatory agencies, such as in the SIENDO Study. Preliminary, interim or top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, these early data points should be viewed with caution until the final data are available. Adverse differences between previous preliminary or interim data and future interim or final data could significantly harm our business.
In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is typically selected from a more extensive amount of available information. Furthermore, we may report interim analyses of only certain endpoints rather than all endpoints. Investors may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product, product candidate or our business.

If the interim or top-line data that we report differ from future or more comprehensive data, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for and commercialize our product candidates, our business, operating results, prospects, or financial condition may be harmed.

***We may not be successful in our efforts to identify or discover additional potential product candidates, or our decisions to prioritize the development of certain product candidates over others may later prove wrong.***

Part of our strategy involves identifying and developing product candidates to build a pipeline of product candidates. Our drug discovery efforts may not be successful in identifying compounds that are useful in treating cancer or other diseases. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential product candidates;
- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval and/or achieve market acceptance; or
- potential product candidates may not be effective in treating their targeted diseases.

We are currently advancing multiple clinical development studies of selinexor, which may create a strain on our limited human and financial resources. As a result, we may not be able to provide sufficient resources to any single product candidate to permit the successful development and commercialization of such product candidate, which could result in material harm to our business. Further, because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. For example, in January 2024, we announced that further clinical development of our eltanexor program is on hold in an effort to focus our resources on our prioritized late-stage programs. 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 for specific indications may not yield any additional commercially-viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

***If we are unable to maintain or expand our sales, marketing and distribution capabilities, we may not be successful in commercializing XPOVIO or any of our products or product candidates, if approved, that we may acquire or develop.***

We have built a commercial infrastructure in the U.S. for XPOVIO, our first commercial product, in hematological malignancies and our company did not previously have any prior experience in the sales, marketing or distribution of pharmaceutical drugs. If XPOVIO or any of our product candidates is approved for additional indications beyond hematological malignancies, such as solid tumors, we may need to evolve our sales, marketing and distribution capabilities and we may not be able to do so successfully or on a timely basis. In the future, we may choose to expand our sales, marketing and distribution infrastructure to market or co-promote one or more of our product candidates, if and when they are approved, or enter into additional collaborations with respect to the sale, marketing and distribution of our product candidates. We are working with existing and potential partners to establish the commercial infrastructure to support the sale of selinexor outside of the U.S. For example, we entered into a license agreement with the Menarini Group ("Menarini") in December 2021, and as amended in March 2023, to, among other things, develop and commercialize NEXPOVIO®(selinexor) for all human oncology indications in Europe (including the United Kingdom ("UK")), Latin America, certain Middle East and Africa regions and other key countries. For additional risks associated with commercializing our products outside of the U.S., please see the risk factor entitled "*We depend on collaborations with third parties for certain aspects of the development, marketing and/or commercialization of XPOVIO and/or our product candidates. If those collaborations are not successful, or if we are not able to maintain our existing collaborations or establish additional collaborations, we may have to alter our development and commercialization plans and may not be able to capitalize on the market potential of XPOVIO or our product candidates*" below.

There are risks involved with establishing and maintaining our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any commercial launch of a product candidate or negatively impact ongoing commercialization efforts for our approved products. Further, we may underestimate the size of the sales force required for a successful product launch and we may need to expand our sales force earlier and at a higher cost than we anticipated. If the commercial launch of any of our product candidates is delayed or does not occur for any reason, including if we do not receive marketing approval in the timeframe we expect, we may have prematurely or unnecessarily incurred commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.
Factors that may inhibit our efforts to successfully commercialize XPOVIO or any product candidates, if approved, on our own include:

- existing or new competitors taking share from XPOVIO or any other future product or preventing XPOVIO or any other future product from gaining share in its approved indications;
- our inability to recruit, train and retain adequate numbers of effective sales, market access, market analytics, operations and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe current or future products;
- the lack of complementary drugs, which may put us at a competitive disadvantage relative to companies with more extensive drug lines;
- unforeseen costs and expenses associated with creating an independent sales, marketing and distribution organization;
- our inability to obtain sufficient coverage and reimbursement from third-party payors and governmental agencies; and
- our ability to supply sufficient inventory of our products for commercial sale.

***Even if we, or our collaborators, are able to effectively commercialize XPOVIO or any approved products that we may develop or acquire, the products may not receive coverage or may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, all of which would harm our business.***

The legislation and regulations that govern marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. As a result, we or our collaborators might obtain marketing approval for a drug in a particular country, but then be subject to price regulations that delay the commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we, or our collaborators, are able to generate from product sales in that country. In the U.S., approval and reimbursement decisions are not linked directly, but there is increasing scrutiny from the Congress, regulatory authorities, payers, patients and pathway organizations of the pricing of pharmaceutical products. Adverse pricing limitations may also hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our, and our collaborators', ability to successfully commercialize XPOVIO and any other products that we may develop or acquire will depend, in part, on the extent to which reimbursement for these products is available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. Obtaining and maintaining adequate reimbursement for XPOVIO and any of our product candidates, if approved, may be difficult. Moreover, the process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price of a product or for establishing the reimbursement rate that such a payor will pay for the product. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for our products. Even with payer coverage, patients may be unwilling or unable to pay the copay required and may choose not to take XPOVIO.

A primary trend in the healthcare industry in the U.S. and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Third-party payors may also seek, with respect to an approved product, additional clinical evidence that goes beyond the data required to obtain marketing approval. They may require such evidence to demonstrate clinical benefits and value in specific patient populations or they may call for costly pharmaceutical studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies before covering our products. Accordingly, we cannot be sure that reimbursement will be or will continue to be available for XPOVIO and any product that we, or our collaborators, commercialize and, if reimbursement is available, we cannot be sure as to the level of reimbursement and whether it will be adequate. Coverage and reimbursement may impact the demand for or the price of XPOVIO or any product candidate for which we, or our collaborators, obtain marketing approval. If reimbursement is not available or is available only at limited levels, we, or our collaborators, may not be able to successfully commercialize XPOVIO or any other approved products.

There may be significant delays in obtaining reimbursement for newly-approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved drugs that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize our products and our overall financial condition.

***Product liability lawsuits against us could divert our resources, cause us to incur substantial liabilities and limit commercialization of XPOVIO or any other products that we may develop or acquire.***

We face an inherent risk of product liability exposure related to our commercialization of XPOVIO and the testing of our product candidates in human clinical trials as the administration of our products to humans may expose us to liability claims, whether or not our products are actually at fault for causing any harm or injury. As XPOVIO is used over longer periods of time by a wider group of patients taking numerous other medicines or by patients with additional underlying conditions, the likelihood of adverse drug reactions or unintended side effects, including death, may increase. For example, we may be sued if any drug we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the

product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against claims that our products or product candidates caused injuries, we will incur substantial liabilities or be required to limit commercialization of our products. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for XPOVIO and any other products that we may develop or acquire;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to successfully commercialize XPOVIO and any other products that we may develop or acquire.

We currently hold clinical trial and general product liability insurance coverage, but that coverage may not be adequate to cover any and all liabilities that we may incur. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

***The business that we or our collaborators conduct outside of the U.S. may be adversely affected by international risks and uncertainties.***

Although our operations are primarily based in the U.S., we and our collaborators conduct business outside of the U.S. and expect to continue to do so in the future. For instance, many of the sites at which our clinical trials are being conducted are located outside of the U.S. In addition, we and our collaborators are seeking and continue to plan to seek approvals to sell our and their products in foreign countries. Any business that we, or our collaborators, conduct outside of the U.S. is subject to additional risks that may materially adversely affect our or their ability to conduct business in international markets, including:

- potentially reduced protection of our intellectual property rights;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market (with low or lower prices) rather than buying them locally;
- unexpected changes in tariffs, trade barriers or regulatory requirements;
- economic weakness, including the uncertainty associated with worldwide economic conditions as a result of inflation, sustained high interest rates, natural disasters and military conflicts, including the conflict between Russia and Ukraine, the war between Israel and Hamas, the Palestinian group that controls the Gaza Strip, volatility in currency exchange rates, pandemics or other public health emergencies, or political instability in particular foreign economies and markets;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- production shortages resulting from any events affecting a product candidate and/or finished drug product supply or manufacturing capabilities abroad;
- business interruptions resulting from geo-political actions, including war and terrorism, such as the ongoing conflict between Russia and Ukraine, the war between Israel and Hamas, pandemics or other public health emergencies, climate change or natural disasters, including earthquakes, hurricanes, typhoons, floods and fires; and
- failure to comply with Office of Foreign Asset Control rules and regulations and the Foreign Corrupt Practices Act (“FCPA”).

**Risks Related to Regulatory Matters**

***Even if we, or our collaborators, complete the necessary preclinical studies and clinical trials for our product candidates, the regulatory approval process is expensive, time-consuming and uncertain and we or they may not receive approvals for the commercialization of some or all of our or their product candidates in a timely manner, or at all.***

Our long-term success and ability to sustain and grow revenue depends on our and our collaborators' ability to continue to successfully develop our product candidates and obtain regulatory approval to market our or their products both in and outside of the U.S. In order to market and sell our products in the EU and many other jurisdictions, we and our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The FDA and comparable foreign regulatory authorities, whose laws and regulations may differ from country to country, impose substantial requirements on the development of product candidates to become eligible for marketing approval and have substantial discretion in the process and may refuse to accept any application or may decide that the data are insufficient for approval and require additional preclinical studies, clinical trials or other studies and testing. The time required to obtain approval outside of the U.S. may differ substantially from that required to obtain FDA approval. For example, in many countries outside of the U.S., it is required that the drug be approved for reimbursement before the drug can be approved for sale in that country. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside of the U.S. does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in other countries. For additional risks related to conducting business outside of the U.S., please see the risk factor above entitled "*The business that we or our collaborators conduct outside of the U.S. may be adversely affected by international risks and uncertainties*."

In addition, the FDA and foreign regulatory authorities retain broad discretion in evaluating the results of our clinical trials and in determining whether the results demonstrate that selinexor or any other product candidate is safe and effective. If we are required to conduct additional clinical trials of selinexor or other product candidates prior to approval of additional indications, in earlier lines of therapy or in combination with other drugs, including additional earlier phase clinical trials that may be required prior to commencing any later phase clinical trials, or additional clinical trials following completion of our current and planned later phase clinical trials, we may need substantial additional funds, and there is no assurance that the results of any such additional clinical trials will be sufficient for approval.

The process of obtaining marketing approvals, both in the U.S. and abroad, is lengthy, expensive and uncertain. It may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information, including manufacturing information, to regulatory authorities for each therapeutic indication to establish the product candidate's safety and effectiveness. 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 product application, may cause delays in the approval or rejection of an application.

The FDA or other regulatory authorities may determine that (i) our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use; (ii) the dose used in a clinical trial has not been optimized and require us to conduct additional dose optimization studies; or (iii) the comparator arm in a trial is no longer the appropriate comparator due to the evolution of the competitive landscape or subsequent data of the comparator product, even if the FDA or other regulatory authority had previously approved the trial design, and we may be required to amend the trial or we may not receive approval of the indication. For example, the FDA's Oncology Center of Excellence has a number of projects to advance the development and regulation of medical products for patients with cancer, such as Project Optimus to reform the dose optimization and dose selection paradigm in oncology drug development to emphasize selection of an optimal dose. These projects may require sponsors to spend additional time and resources either pre- or post-approval, and our ability to complete existing trials or initiate new trials may be delayed.

Further, under the Pediatric Research Equity Act ("PREA"), an NDA or supplement to an NDA for certain drugs must contain data to assess the safety and effectiveness of the drug in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless the sponsor receives a deferral or waiver from the FDA. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. The law requires the FDA to send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. It further requires the FDA to publicly post the PREA Non-Compliance letter and sponsor's response. The applicable legislation in the EU also requires sponsors to either conduct clinical trials in a pediatric population in accordance with a Pediatric Investigation Plan approved by the Pediatric Committee of the European Medicines Agency ("EMA") or to obtain a waiver or deferral from the conduct of these studies by this Committee. For any of our product candidates for which we

or our collaborators are seeking regulatory approval in the U.S. or the EU, we cannot guarantee that we will be able to obtain a waiver or alternatively complete any required studies and other requirements in a timely manner, or at all, which could result in an issuance and publication of a PREA Non-Compliance letter and associated reputational harm, our product candidate being considered misbranded and subject to relevant enforcement action, invalidation of the marketing application, and/or financial penalties. Our collaborators are also subject to similar requirements outside of the U.S. and the EU and thus the attendant risks and uncertainties.

Finally, our ability to develop and market new drug products may be threatened by ongoing litigation challenging the FDA's approval of mifepristone. Specifically, on April 7, 2023, the U.S. District Court for the Northern District of Texas invalidated the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various measures adopted under a Risk Evaluation and Mitigation Strategy ("REMS"). In reaching that decision, the district court made a number of findings that numerous representatives of the pharmaceutical and biotechnology industry believe will chill the development, approval and distribution of new drug products in the U.S. Among other determinations, the district court substituted its scientific judgement for that of the FDA and it held that FDA must provide a special justification for any differences between an approved drug's labeling and the conditions that existed in the drug's clinical trials. Further, the district court read the jurisdictional requirements governing litigation in federal court so as to potentially allow virtually any party to bring a lawsuit against the FDA in connection with its decision to approve an NDA or establish requirements under a REMS.

On April 13, 2023, the district court decision was stayed, in part, by the U.S. Court of Appeals for the Fifth Circuit. Thereafter, on April 21, 2023, the U.S. Supreme Court entered a stay pending disposition of the appeal of the district court decision in the Court of Appeals for the Fifth Circuit or the Supreme Court. The Court of Appeals for the Fifth Circuit held oral arguments in the case on May 17, 2023 and, on August 16, 2023, issued its decision. The Court of Appeals declined to order the removal of mifepristone from the market, finding that a challenge to the FDA's initial approval in 2000 is barred by the statute of limitations. However, the Court of Appeals did hold that changes allowing for expanded access of mifepristone that the FDA authorized in 2016 and 2021 were arbitrary and capricious in violation of federal law. On September 8, 2023, the Department of Justice (the "DOJ") and a manufacturer of mifepristone asked the U.S. Supreme Court to review the Court of Appeals' decision. On December 12, 2023, the Supreme Court announced that it will review the Court of Appeals' decision. The Supreme Court heard oral arguments in this case on March 26, 2024, and a decision is expected in July 2024.

Depending on the outcome of this litigation and the regulatory uncertainty it has engendered, our ability to develop new drug product candidates and to maintain approval of existing drug products and measures adopted under a REMS is at risk and our efforts to develop and market new drug products could be delayed, undermined or subject to protracted litigation.

The approval of our and our collaborators' current or future product candidates for commercial sale could be delayed, limited or denied or we or they may be required to conduct additional studies for a number of reasons, including, but not limited to, the following:

- regulatory authorities may determine that our or our collaborators' product candidates do not demonstrate safety and effectiveness in accordance with regulatory agency standards based on a number of considerations, including AEs that are reported during clinical trials;
- regulatory authorities could analyze and/or interpret data from clinical trials and preclinical testing in different ways than we, or our collaborators, interpret them and determine that our data is insufficient for approval;
- regulatory authorities may require more information, including additional preclinical or clinical data or trials, to support approval, as in the case of our new trial for selinexor in endometrial cancer following discussions with the FDA in early 2022 on our SIENDO Study;
- regulatory authorities could determine that our manufacturing processes are not properly designed, are not conducted in accordance with federal or other laws or otherwise not properly managed, and we may be unable to obtain regulatory approval for a commercially viable manufacturing process for our product candidates in a timely manner, or at all;
- the supply or quality of our or our collaborators' product candidates for our clinical trials may be insufficient, inadequate or delayed;
- the size of the patient population required to establish the efficacy of our or our collaborators' product candidates to the satisfaction of regulatory agencies may be larger than we or they anticipated;
- our failure or the failure of clinical investigational sites and the records kept at the respective locations, including clinical trial data, to be in compliance with the FDA's current good clinical practices regulations ("GCP") or comparable regulations outside of the U.S., including the failure to pass inspections of our corporate site or our clinical trial sites;
- regulatory authorities may change their approval policies or adopt new regulations;

- regulatory authorities may not be able to undertake reviews, applicable inspections or approval processes in a timely manner;
- the results of our earlier clinical trials may not be representative of our future, larger trials;
- regulatory authorities may not agree with our or our collaborators' regulatory approval strategies or components of our or their regulatory filings, such as the design or implementation of the relevant clinical trials; or
- a product may not be approved for the indications that we, or our collaborators, request or may be limited or subject to restrictions or post-approval commitments that render the approved drug not commercially viable.

Finally, we or our collaborators could face heightened risks with respect to seeking marketing approval in the UK as a result of the withdrawal of the UK from the EU, commonly referred to as Brexit. The UK is no longer part of the European Single Market and EU Customs Union. As of January 1, 2021, the MHRA became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland will continue to be subject to EU rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended) ("HMR") as the basis for regulating medicines. The HMR has incorporated into the domestic law of the body of EU law instruments governing medicinal products that pre-existed prior to the UK's withdrawal from the EU. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us or our collaborators to restrict or delay efforts to seek regulatory approval in the UK for our or their product candidates, which could significantly and materially harm our business.

Since a significant proportion of the regulatory framework for pharmaceutical products in the UK covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit may have a material impact upon the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the UK. For example, the UK is no longer covered by the centralized procedures for obtaining EU-wide marketing authorization from the EMA, and a separate marketing authorization will be required to market our product candidates in the UK. Until December 31, 2023, it was possible for the MHRA to rely on a decision taken by the European Commission ("EC") on the approval of a new marketing authorization via the centralized procedure. From January 1, 2024 on, a new international recognition procedure ("IRP") applies, which intends to facilitate approval of pharmaceutical products in the UK. The IRP is open to applicants that have already received an authorization for the same product from one of the MHRA's specified Reference Regulators ("RRs"). The RRs notably include EMA and regulators in the EU/European Economic Area ("EEA") member states for approvals in the EU centralized procedure and mutual recognition procedure as well as the FDA (for product approvals granted in the U.S.). However, the concrete functioning of the IRP is currently unclear. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us or our collaborators to restrict or delay efforts to seek regulatory approval in the UK for our product candidates, which could significantly and materially harm our business.

We, or our collaborators, may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our or their products in any market. Any failure, delay or setback in obtaining regulatory approval for our or our collaborators' product candidates could materially adversely affect our or our collaborators' ability to generate revenue from a particular product candidate, which could result in significant harm to our financial position and adversely impact our stock price.

***We, or our collaborators, may seek approval from the FDA or comparable foreign regulatory authorities to use accelerated development pathways for our product candidates. If we, or our collaborators, are not able to use such pathways, we, or they, may be required to conduct additional clinical trials beyond those that are contemplated, which would increase the expense of obtaining, and delay the receipt of, necessary marketing approvals, if we, or they, receive them at all. In addition, even if an accelerated approval pathway is available to us, or our collaborators, it may not lead to expedited approval of our product candidates, or approval at all.***

Under the Federal Food, Drug and Cosmetic Act ("FDCA") and implementing regulations, the FDA may grant accelerated approval to a product candidate to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies, upon a determination that the product has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available

therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. Similar risks to those described above are also applicable to any application that we, or our collaborators, have submitted or may submit in other jurisdictions outside of the U.S. Prior to seeking such accelerated approval, we, or our collaborators, will continue to seek feedback from the FDA or comparable foreign regulatory agencies and otherwise evaluate our, or their, ability to seek and receive such accelerated approval.

There can be no assurance that the FDA or foreign regulatory agencies will agree with our, or our collaborators', surrogate endpoints or intermediate clinical endpoints in any of our, or their, clinical trials, or that we, or our collaborators, will decide to pursue or submit any additional New Drug Applications ("NDA") for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that, after feedback from the FDA or comparable foreign regulatory agencies, we, or our collaborators, will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval. Furthermore, for any submission of an application for accelerated approval or application under another expedited regulatory designation, there can be no assurance that such submission or application will be accepted for filing or that any expedited development, review or approval will be granted on a timely basis, or at all.

Finally, there can be no assurance that we will satisfy all FDA requirements, including new provisions, that govern accelerated approval. For example, with passage of the FDORA in December 2022, Congress modified certain provisions governing accelerated approval of drug and biologic products. Specifically, the new legislation authorized the FDA to (i) require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded; (ii) require a sponsor of a product granted accelerated approval to submit progress reports on its post-approval studies to FDA every six months until the study is completed; and (iii) use expedited procedures to withdraw accelerated approval of an NDA or a Biologic License Application after the confirmatory trial fails to verify the product's clinical benefit. Further, FDORA requires the agency to publish on its website "the rationale for why a post-approval study is not appropriate or necessary" whenever it decides not to require such a study upon granting accelerated approval. We will need to fully comply with these and other requirements in connection with the development and approval of any product candidate that qualifies for accelerated approval.

In March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. The FDA indicated that the accelerated approval pathway is commonly used for approval of oncology drugs due to the serious and life-threatening nature of cancer. Although single-arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust efficacy and safety assessment and allows for direct comparisons to an available therapy. To that end, the FDA outlined considerations for designing, conducting, and analyzing data for trials intended to support accelerated approvals of oncology therapeutics. While this guidance is currently only in draft form and will ultimately not be legally binding even when finalized, we will need to observe the FDA's guidance closely to ensure that our products qualify for accelerated approval.

Accordingly, a failure to obtain and maintain accelerated approval or any other form of expedited development, review or approval for our product candidates, or withdrawal of a product candidate, would result in a longer time period until commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

***XPOVIO and any of our product candidates for which we, or our collaborators, obtain marketing approval in the future are subject to post-marketing regulatory requirements, including following accelerated or conditional approvals of our product candidates, and could be subject to post-marketing restrictions or withdrawal from the market, and we, and our collaborators, may be subject to substantial penalties if we, or they, fail to comply with regulatory requirements or if we, or they, experience unanticipated problems with our products following approval.***

Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. XPOVIO and any of our product candidates for which we, or our collaborators, obtain marketing approval in the future, as well as the manufacturing processes, post-approval studies and measures, labeling, advertising and promotional activities for such drug, among other things, will be subject to continual requirements of and review by the FDA and other U.S. and foreign regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. For example, as a condition of the XPOVIO approval by the FDA for the multiple myeloma and DLBCL indications, we are required to complete certain post-marketing commitments. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the drug may be marketed or to the conditions of approval, including the requirement to implement a REMS, which could include requirements for a restricted distribution system.

The FDA also imposes requirements for costly post-marketing studies or clinical trials to maintain approval of any products that received accelerated or conditional approval. For drugs approved under the FDA's Accelerated Approval Program, the FDA typically requires post-marketing confirmatory trials to evaluate the anticipated effect on irreversible morbidity or mortality or other clinical benefit. These confirmatory trials must be completed with due diligence. For example, in June 2020, the FDA approved XPOVIO to treat DLBCL under the FDA's accelerated approval regulations and as a condition of the accelerated approval for this indication we are required to comply with a number of post-approval requirements. We may not be able to successfully and timely complete these post-approval requirements or any other post-marketing confirmatory study as required to maintain approval or achieve full approval of our products. If required post-approval studies fail to verify the clinical benefits of our products or confirm that the surrogate marker used for accelerated approval of our products showed an adequate correlation with clinical outcomes, if a sufficient number of participants cannot be enrolled, or if we fail to perform the required post-approval studies with due diligence or on a timely basis, the FDA has the authority to withdraw approval of the drug following a hearing conducted under the FDA's regulations, which could have a material adverse impact on our business. We cannot be certain of the results of the confirmatory clinical studies for the DLBCL indication or any other future conditional approval we receive or what action the FDA may take if the results of those studies are not as expected based on clinical data that FDA has already reviewed.

Similar risks to those described above are also applicable to any application that we, or our collaborators, have submitted or may submit in other jurisdictions outside of the U.S., including applications submitted to the EMA to support approval of selinexor to treat heavily pretreated multiple myeloma, relapsed or refractory DLBCL, or any other cancer indication. For medicinal products where the benefit of immediate availability outweighs the risk of less comprehensive data than normally required, based on the scope and criteria defined in legislation and guidelines, it is possible to obtain a conditional marketing authorization in the EU with a 12-month validity period and annual renewal pursuant to Regulation No 507/2006. These are granted only if the EMA's Committee for Medicinal Products for Human Use ("CHMP") finds that all four of the following requirements are met: (i) the benefit-risk balance of the product is positive; (ii) it is likely that the sponsor will be able to provide comprehensive data; (iii) unmet medical needs will be fulfilled; and (iv) the benefit to public health of the medicinal product's immediate availability on the market outweighs the risks due to the need for further data.

Once a conditional marketing authorization has been granted, the marketing authorization holder must fulfil specific obligations within defined timelines. These obligations could include completing ongoing or new studies or collecting additional data to confirm the medicine's benefit-risk balance remains positive. For example, the July 2022 marketing authorization from the EC for NEXPOVIO to treat adult patients with multiple myeloma after at least one prior therapy satisfied the conditional approval obligation for NEXPOVIO for patients with multiple myeloma who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, two immunomodulatory agents, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy. Conditional marketing authorization is valid for a period of one year and can be renewed/prolonged if the conditions set out in the conditional marketing authorization are met. Further, as discussed above, under FDORA, modifications to regulations governing accelerated approval require a sponsor to have the confirmatory clinical trial underway before accelerated approval is awarded as well as other requirements following accelerated approval. If we, or our collaborators, are not able to fulfill the specific obligations set out in any conditional marketing authorization requirements, the conditional marketing authorization may not be prolonged and we, or our collaborators, will no longer be able to market the product for the indication receiving conditional approval.

The FDA and comparable foreign regulatory authorities may also impose requirements for costly surveillance to monitor the safety or efficacy of an approved drug. The FDA and other U.S. or foreign agencies, including the DOJ, closely regulate and monitor the post-approval marketing and promotion of drugs to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use, and if we, or our collaborators communicate about any of our product candidates for which we, or they, receive marketing approval in a way that regulators assert goes beyond their approved indications, we, or they, may be subject to warnings or enforcement action for off-label marketing. Alleged violations of the FDCA or other statutes, including the False Claims Act (the "FCA"), relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.
We will need to carefully navigate the FDA's various regulations, guidance and policies, along with recently enacted legislation, to ensure compliance with restrictions governing promotion of our products. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug or biologic. Moreover, with passage of the Pre-Approval Information Exchange Act in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. In addition, in October 2023, the FDA published draft guidance outlining the agency's non-binding policies governing the distribution of scientific information on unapproved uses to healthcare providers. This draft guidance calls for such communications to be truthful, non-misleading, factual, and unbiased and include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive requirements by the FDA and comparable foreign regulatory authorities, including ensuring that quality control and manufacturing procedures conform to current Good Manufacturing Practice ("cGMP"), which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, our collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA or foreign regulatory authorities to monitor and ensure compliance with cGMPs or other regulations.

Post-approval discovery of previously unknown problems with our products, including AEs of unanticipated severity or frequency, or relating to our manufacturing processes, data integrity issues with regulatory filings, or failure to comply with regulatory requirements, may yield various results, including:

- litigation involving patients taking our drug;
- restrictions on our manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of our products;
- restrictions on the distribution or use of our products;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal, recall or seizure of our products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with our current or potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products; or
- injunctions or the imposition of civil or criminal penalties.

Similar restrictions apply to the approval of our products in the EU. The holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- compliance with the EU's stringent pharmacovigilance or safety reporting rules, which can impose post-authorization studies and additional monitoring obligations;
- the manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the EC Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU; and
- the marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the EU notably under Directive 2001/83/EC, as amended, and are also subject to EU Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the EU.

Finally, we or our collaborators are also subject to other regulations in various jurisdictions, including the Drug Supply Chain Security Act (the "DSCSA") in the U.S., the Falsified Medicines Directive in the EU and similar laws and regulations in other countries that require us or them to develop electronic systems to serialize, track, trace and authenticate units of our products through the supply chain and distribution system. Compliance with these regulations may result in increased expenses for us or our collaborators or impose greater administrative burdens on our or their organizations, and any failure on our or our collaborators' part to meet these requirements could result in fines or other penalties or reputational harm.

Accordingly, in connection with our currently approved products and assuming we, or our collaborators, receive marketing approval for one or more of our product candidates, we, and our collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we, and our collaborators, are not able to comply with post-approval regulatory requirements, our or our collaborators' ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

***If we, or our collaborators, are required by the FDA, EMA or comparable regulatory authority to obtain clearance or approval of a companion diagnostic test in connection with approval of any of our product candidates or a group of therapeutic products, and we or they do not obtain or there are delays in obtaining clearance or approval of a diagnostic test, we may not be able to commercialize the product candidate and our ability to generate revenue may be materially impaired.***

In connection with our ongoing development of a registration-enabling study of selinexor in patients whose endometrial cancer is *TP53*wild-type, we are utilizing a companion diagnostic. To be successful in developing and commercializing product candidates in combination with companion diagnostics, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. According to FDA guidance, if the FDA determines that a companion diagnostic device is essential to ensuring the safety and effectiveness of a novel therapeutic product or new indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic is not also approved or cleared. In certain circumstances (for example, when a therapeutic product is intended to treat a serious or life-threatening condition for which no satisfactory available therapy exists or when the labelling of an approved product needs to be revised to address a serious safety issue), however, the FDA may approve a therapeutic product without the prior or contemporaneous marketing authorization of a companion diagnostic. In this case, approval of a companion diagnostic may be a post-marketing requirement or commitment.

If the FDA requires clearance or approval of a companion diagnostic for any of our product candidates, whether before, concurrently with approval, or post-approval of the product candidate, we, and/or our collaborators, may encounter difficulties in developing and obtaining clearance or approval for these companion diagnostics. The process of obtaining or creating such diagnostic is time consuming and costly. The FDA previously has required in vitro companion diagnostics intended to select the patients who will respond to a product candidate to obtain pre-market approval ("PMA"), simultaneously with approval of the therapeutic candidate.

The PMA process, including the gathering of preclinical and clinical data and the submission and review by the FDA, can take several years or longer. It involves a rigorous pre-market review during which the sponsor must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing, and labeling. After a device is placed on the market, it remains subject to significant regulatory requirements, including requirements governing development, testing, manufacturing, distribution, marketing, promotion, labeling, import, export, record-keeping, and adverse event reporting. Similar risks to those described above are also applicable to any companion diagnostic that we, or our collaborators, utilize in our clinical trials in connection with approval of a product candidate outside of the U.S. For example, in the EU, until May 25, 2022, in vitro diagnostic medical devices were regulated by Directive 98/79/EC (the "IVDD"), which has been repealed and replaced by Regulation (EU) No 2017/746 (the "IVDR"). The regulation of companion diagnostics is now subject to further requirements set forth in the IVDR. Companion diagnostics will have to undergo a conformity assessment by a notified body. Before it can issue an EU certificate, the notified body must seek a scientific opinion from the EMA on the suitability of the companion diagnostic to the medicinal product concerned if the medicinal product falls exclusively within the scope of the centralized procedure for the authorization of medicines, or the medicinal product is already authorized through the centralized procedure, or a marketing authorization application for the medicinal product has been submitted through the centralized procedure. As part of the process to obtain a CE-mark for the FMI FoundationOne®CDx for the purpose of determining *TP53*wild-type status for use of selinexor in the maintenance treatment of *TP53* wild-type endometrial cancer patients, a performance study is required which leverages our global, Phase 3 trial evaluating selinexor as a maintenance therapy following systemic therapy in patients with *TP53* wild-type advanced or recurrent endometrial cancer (the "EC-042 Study") (e.g., using the unapproved FoundationOne®CDx IVD to screen for *TP53* wild-type patients in the EC-042 Study and using the data generated to validate the CDx itself). As the regulations are relatively new, the industry is gaining experience in the compilation of these submissions while the national Competent Authorities and the respective Ethics Committees are also gaining expertise in assessing these applications. As a result, the assessment deadlines of these performance study submissions and amendments are often not met. These new regulations have and could continue to negatively impact the pace of enrollment in our clinical trials. For example, in 2023, site activation for our Phase 3 clinical trial in endometrial cancer was delayed in the EU due to the new IVDR regulations. Consequently, the ability to use the FoundationOne®CDx in vitro diagnostic medical devices to screen patients for *TP53* status in the EC-042 Study has been delayed in various countries in the EU.

We may rely on third parties for the design, development and manufacture of companion diagnostic tests for our product candidates, such as in the case of our ongoing Phase 3 trial evaluating selinexor in patients with TP53wild-type advanced or recurrent endometrial cancer. If we enter into such collaborative agreements, we will be dependent on the sustained cooperation and effort of our future collaborators in developing and obtaining clearance or approval for these companion diagnostics. It may be necessary to resolve issues such as selectivity/specificity, analytical validation, reproducibility, or clinical validation of companion diagnostics during the development and regulatory clearance or approval processes. Moreover, even if data from preclinical studies and early clinical trials appear to support development of a companion diagnostic for a product candidate, data generated in later clinical trials may fail to support the analytical and clinical validation of the companion diagnostic. We and our future collaborators may encounter difficulties in developing, obtaining regulatory clearance or approval for, manufacturing and commercializing companion diagnostics similar to those we face with respect to our product candidates themselves, including issues with achieving regulatory clearance or approval, production of sufficient quantities at commercial scale and with appropriate quality standards, and in gaining market acceptance.

If we are unable to successfully develop companion diagnostics for our product candidates, or experience delays in doing so, the development of our product candidates may be adversely affected, our product candidates may not obtain marketing approval, and we may not realize the full commercial potential of any of our product candidates that obtain marketing approval. As a result, our business, results of operations and financial condition could be materially harmed. In addition, a diagnostic company with whom we contract may decide to discontinue selling or manufacturing the companion diagnostic test that we anticipate using in connection with development and commercialization of product candidates or our relationship with such diagnostic company may otherwise terminate. We may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our product candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the co-development or commercialization of our companion diagnostic and therapeutic product candidates.

***We or our collaborators may seek certain designations for our product candidates in or outside of the U.S., including Breakthrough Therapy, Fast Track and Priority Review designations, and PRIME Designation in the EU, but we, or they, might not receive such designations, and even if we, or they, do, such designations may not lead to a faster development or regulatory review or approval process.***

We may seek certain designations for one or more of our product candidates that could expedite review and approval by the FDA. A Breakthrough Therapy product is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For products that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens.

The FDA may also designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective.

We may also seek a Priority Review designation for one or more of our product candidates. If the FDA determines that a product candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the product candidate for priority review. A Priority Review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months.

These designations are within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for these designations, the FDA may disagree and instead determine not to make such designation. Further, even if we receive a designation, such as the recent receipt of Fast Track designation for selinexor to treat myelofibrosis, the receipt of such designation for a product candidate may not result in a faster development or regulatory review or approval process compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualifies for these designations, the FDA may later decide that the product candidates no longer meet the conditions for qualification and rescind the designation or decide that the time period for FDA review or approval will not be shortened.

In the EU, we or our collaborators may seek PRIME designation for some of our product candidates in the future. PRIME is a voluntary program aimed at enhancing the EMA's role to reinforce scientific and regulatory support in order to optimize development and enable accelerated assessment of new medicines that are of major public health interest with the potential to address unmet medical needs. The program focuses on medicines that target conditions for which there exists no satisfactory method of treatment in the EU or even if such a method exists, it may offer a major therapeutic advantage over existing treatments. PRIME is limited to medicines under development and not authorized in the EU and the sponsor intends to apply for an initial MAA through the centralized procedure. To be accepted for PRIME, a product candidate must meet the eligibility criteria with respect to its major public health interest and therapeutic innovation based on information that is capable of substantiating the claims. The benefits of a PRIME designation include the appointment of a CHMP rapporteur to provide continued support and help to build knowledge ahead of a MAA, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review, meaning reduction in the review time for an opinion on approvability to be issued earlier in the application process. PRIME enables a sponsor to request parallel EMA scientific advice and health technology assessment advice to facilitate timely market access. Even if we or our collaborators receive PRIME designation for any of our product candidates, the designation may not result in a materially faster development process, review or approval compared to conventional EMA procedures. Further, obtaining PRIME designation does not assure or increase the likelihood of the EMA's grant of a marketing authorization.

***We, or our collaborators, may not be able to obtain orphan drug exclusivity for any product candidates we, or they, may develop, and even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products.***

Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition. A similar regulatory scheme governs approval of orphan products by the EMA in the EU. Generally, if a product candidate with an Orphan Drug Designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA, as applicable, from approving another marketing application for the same product for the same therapeutic indication for that time period. The applicable period is seven years in the U.S. and ten years in the EU. The exclusivity period in the EU can be reduced to six years if a product no longer meets the criteria for Orphan Drug Designation, in particular if the product is sufficiently profitable so that market exclusivity is no longer justified.

In order for the FDA to grant orphan drug exclusivity to one of our products, the agency must find that the product is indicated for the treatment of a condition or disease with a patient population of fewer than 200,000 individuals annually in the U.S. The FDA may conclude that the condition or disease for which we seek orphan drug exclusivity does not meet this standard. Even if we obtain orphan drug exclusivity for a product, such as the recent receipt of orphan drug exclusivity for selinexor for the treatment of myelofibrosis, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA and comparable foreign regulatory authorities, such as the EMA, can subsequently approve the same product for the same condition if the FDA or such other authorities conclude that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may also be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition.

In 2017, the Congress passed the FDA Reauthorization Act of 2017 (the "FDARA"). The FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. Under omnibus legislation signed by former President Trump in December 2020, the requirement for a product to show clinical superiority applies to drugs and biologics that received Orphan Drug Designation before the enactment of the FDARA in 2017, but have not yet been approved or licensed by the FDA.

The FDA and Congress may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the Court of Appeals for the 11th Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term "same disease or condition" means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, the FDA announced that, in matters beyond the scope of that court order, the FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved.

We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future or whether Congress will take legislative action, and it is uncertain how any changes might affect our business. Depending on what changes the FDA or Congress may make to orphan drug regulations and policies, our business could be adversely impacted.

***Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.***

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

***Current and future legislation may increase the difficulty and cost for us, or any collaborators, to obtain marketing approval and commercialize our or their product candidates, if approved, and affect the prices we, or they, may obtain.***

In the U.S. and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our or our collaborators' product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any collaborators, to profitably sell or commercialize XPOVIO or any product candidate for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any collaborators, may receive for any approved products. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act (collectively the "PPACA"). In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Further, with the passage of the Inflation Reduction Act (the "IRA") in August 2022, Congress extended the expansion of PPACA premium tax credits through 2025.

These and other laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our products or product candidates for which we may obtain regulatory approval or the frequency with which any such product is prescribed or used. For example, the Consolidated Appropriations Act, which was signed into law by President Biden in December 2022, made several changes to sequestration of the Medicare program. Section 1001 of the Act delays the 4% Statutory Pay-As-You-Go Act of 2010 sequester for two years, through the end of calendar year 2024. Triggered by enactment of the American Rescue Plan Act of 2021, the 4% cut to the Medicare program would have taken effect in January 2023. The Act's health care offset title includes Section 4163, which extends the 2% Budget Control Act of 2011 Medicare sequester for six months into fiscal year 2032 and lowers the payment reduction percentages in fiscal years 2030 and 2031.

Since enactment of the PPACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with the enactment of the Tax Cuts and Jobs Act of 2017 (the "TCJA"), Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, in December 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the PPACA is an essential and inseverable feature of the PPACA, and therefore because

the mandate was repealed as part of the TCJA, the remaining provisions of the PPACA are invalid as well. In June 2021, the U.S. Supreme Court dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the PPACA. Litigation and legislation over the PPACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the PPACA, including directing federal agencies with authorities and responsibilities under the PPACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the PPACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In January 2021, however, President Biden issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Executive Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the PPACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the health insurance marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the PPACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria and new payment methodologies that govern XPOVIO or any other approved product and/or the level of reimbursement physicians receive for administering XPOVIO or any other approved product we, or our collaborators, might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from XPOVIO or from product candidates for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates.

***The prices of prescription pharmaceuticals in the U.S. and foreign jurisdictions are subject to considerable legislative and executive actions and could impact the prices we obtain for our products, if and when licensed.***

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the U.S. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, former President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, the Centers for Medicare & Medicaid Services ("CMS") issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, the Department of Health and Human Services (the "HHS") and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program to import certain prescription drugs from Canada into the U.S. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America ("PhRMA") but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue the HHS. Nine states (Colorado, Florida, Maine, New Hampshire, New Mexico, North Dakota, Texas, Vermont and Wisconsin) have passed laws allowing for the importation of drugs from Canada. Certain of these states have submitted Section 804 Importation Program proposals and are awaiting FDA approval. On January 5, 2024, the FDA approved Florida's plan for Canadian drug importation.

Further, in November 2020, the HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers. The final rule would also eliminate the current safe harbor for Medicare drug rebates and create new safe harbors for beneficiary point-of-sale discounts and pharmacy benefit manager service fees. It originally was set to go into effect on January 1, 2022, but with passage of the IRA has been delayed by Congress to January 1, 2032.

In July 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. The Order directs the HHS to create a plan within 45 days to combat "excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging." In September 2021, the HHS released its plan to reduce

pharmaceutical prices. The key features of that plan are to: (a) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (b) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

On August 16, 2022, the IRA was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least nine years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated “maximum fair price” under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year.

On June 6, 2023, Merck & Co. filed a lawsuit against the HHS and CMS asserting that, among other things, the IRA’s Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U.S. Chamber of Commerce (the “Chamber”), Bristol Myers Squibb Company, the PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against the HHS and CMS. There have been various decisions by the courts considering these cases since they were filed. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results. Accordingly, while it is currently unclear how the IRA will be effectuated, we cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Finally, outside of the U.S., in some nations, including those of the EU, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we, or our collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies.

These measures, as well as others adopted in the future, may result in additional downward pressure on the price that we receive for XPOVIO or any other approved product we or our collaborators might bring to market. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from XPOVIO or from product candidates that we, or our collaborators, may successfully develop and for which we, or they, may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates.

***Our relationships with healthcare providers, physicians and third-party payers will be subject to applicable anti-kickback, fraud and abuse, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.***

Healthcare professionals, including but not limited to physicians, nurses, medical directors, hospitals, pharmacies, pharmacy benefit managers, group purchasing organizations, wholesalers, insurers, and all individuals employed by such entities (collectively, "HCPs"), may influence the recommendation and prescription of our approved products. Our arrangements with HCPs and others who have the ability to influence the recommendation and prescription of our products may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order, or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;
- the FCA imposes criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting or causing to be presented, to the federal government, claims for payment or approval from Medicare, Medicaid or other government payers that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties;
- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), as further amended by the Health Information Technology for Economic and Clinical Health Act, which imposes certain requirements, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, healthcare clearinghouses and healthcare providers;
- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements under the federal Physician Payment Sunshine Act, which requires manufacturers of drugs, devices, biologics and medical supplies to report to the HHS, information related to payments and other transfers of value to physicians, other healthcare providers and teaching hospitals and ownership and investment interests held by physicians and their immediate family members and applicable group purchasing organizations; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payers, including private insurers, and certain state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures.

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. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, imprisonment and the curtailment or restructuring of our operations, any of which could adversely affect our business, financial condition, results of operations and prospects.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Liabilities they incur

pursuant to these laws could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

***Our reporting and payment obligations under the Medicaid Drug Rebate Program and other governmental drug pricing programs are complex and may involve subjective decisions. Any failure to comply with those obligations could subject us to penalties and sanctions.***

As a condition of reimbursement by various federal and state health insurance programs, we are required to calculate and report certain pricing information to federal and state agencies. The regulations governing the calculations, price reporting and payment obligations are complex and subject to interpretation by various government and regulatory agencies, as well as the courts. Reasonable assumptions have been made where there is lack of regulations or clear guidance and such assumptions involve subjective decisions and estimates. We are required to report any revisions to our calculation, price reporting and payment obligations previously reported or paid. Such revisions could affect our liability to federal and state payers and also adversely impact our reported financial results of operations in the period of such restatement. Further, a number of states have either implemented or are considering implementation of drug price transparency legislation that may prevent or limit our ability to take price increases at certain rates or frequencies. Requirements under such laws include advance notice of planned price increases, reporting price increase amounts and factors considered in taking such increases, wholesale acquisition cost information disclosure to prescribers, purchasers, and state agencies, and new product notice and reporting. Such legislation could limit the price or payment for certain drugs, and a number of states are authorized to impose civil monetary penalties or pursue other enforcement mechanisms against manufacturers for the untimely, inaccurate, or incomplete reporting of drug pricing information or for otherwise failing to comply with drug price transparency requirements. If we are found to have violated state law requirements, we may become subject to significant penalties or other enforcement mechanisms, which could have a material adverse effect on our business.

Uncertainty exists as new laws, regulations, judicial decisions, or new interpretations of existing laws, or regulations related to our calculations, price reporting or payments obligations increases the chances of a legal challenge, restatement or investigation. If we become subject to investigations, restatements, or other inquiries concerning our compliance with price reporting laws and regulations, we could be required to pay or be subject to additional reimbursements, penalties, sanctions or fines, which could have a material adverse effect on our business, financial condition and results of operations. In addition, it is possible that future healthcare reform measures could be adopted, which could result in increased pressure on pricing and reimbursement of our products and thus have an adverse impact on our financial position or business operations.

Further, state Medicaid programs may be slow to invoice pharmaceutical companies for calculated rebates resulting in a lag between the time a sale is recorded and the time the rebate is paid. This results in us having to carry a liability on our consolidated balance sheets for the estimate of rebate claims expected for Medicaid patients. If actual claims are higher than current estimates, our financial position and results of operations could be adversely affected.

In addition to retroactive rebates and the potential for 340B Program refunds, if we are found to have knowingly submitted any false price information related to the Medicaid Drug Rebate Program to CMS, we may be liable for civil monetary penalties. Such failure could also be grounds for CMS to terminate our Medicaid drug rebate agreement, pursuant to which we participate in the Medicaid program. In the event that CMS terminates our rebate agreement, federal payments may not be available under government programs, including Medicaid or Medicare Part B, for our covered outpatient drugs.

Additionally, if we overcharge the government in connection with the Federal Supply Schedule pricing program or Tricare Retail Pharmacy Program, whether due to a misstated Federal Ceiling Price or otherwise, we are required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the FCA and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.
Our collaborators are also subject to similar requirements outside of the U.S. and thus the attendant risks and uncertainties. If our collaborators suffer material and adverse effects from such risks and uncertainties, our rights and benefits for our licensed products could be negatively impacted, which could have a material and adverse impact on our revenues.

***We are subject to stringent privacy laws, information security laws, regulations, policies and contractual obligations related to data privacy and security and changes in such laws, regulations, policies and contractual obligations, and failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.***

We are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of personally-identifying information, which among other things, impose certain requirements relating to the privacy, security and

transmission of personal information, including comprehensive regulatory systems in the U.S., EU, UK and other countries in which we may conduct business. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. Failure to comply with any of these laws and regulations could result in enforcement action against us, including fines, imprisonment of company officials and public censure, claims for damages by affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

There are numerous U.S. federal and state laws and regulations related to the privacy and security of personal information. In particular, regulations promulgated pursuant to HIPAA establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Determining whether protected health information has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation.

If we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties. HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

In addition to potential enforcement by the HHS, we could also be potentially subject to privacy enforcement from the Federal Trade Commission (the “FTC”). The FTC has been particularly focused on the unpermitted processing of health and genetic data through its recent enforcement actions and is expanding the types of privacy violations that it interprets to be “unfair” under Section 5 of the FTC Act, as well as the types of activities it views to trigger the Health Breach Notification Rule (which the FTC also has the authority to enforce). The agency is also in the process of developing rules related to commercial surveillance and data security. We will need to account for the FTC’s evolving rules and guidance for proper privacy and data security practices in order to mitigate risk for a potential enforcement action, which may be costly.

States are also active in creating specific rules relating to the processing of personal information. In 2018, California passed into law the California Consumer Privacy Act (the “CCPA”), which took effect on January 1, 2020 and imposed many requirements on businesses that process the personal information of California residents. Many of the CCPA’s requirements are similar to those found in the European General Data Protection Regulation (the “GDPR”), which is further described below, including requiring businesses to provide notice to data subjects regarding the information collected about them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA also affords California residents the right to opt-out of “sales” of their personal information. The CCPA contains significant penalties for companies that violate its requirements.

In November 2020, California voters passed a ballot initiative for the California Privacy Rights Act (the “CPRA”), which went into effect on January 1, 2023 and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – the sole responsibility of which is to enforce the CPRA and other California privacy laws, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities.

In addition to California, eleven other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of “sensitive” data, which includes health data in some cases. Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or have already passed comprehensive privacy laws during the 2024 legislative sessions that will go into effect in 2025 and beyond, including New Hampshire and New Jersey. Other states will be considering these laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, Washington state passed a health privacy law in 2023 that will regulate the collection and sharing of health information, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data, and more states (such as Vermont) are considering such legislation in 2024. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Similar to the laws in the U.S., there are significant privacy and data security laws that apply in Europe and other countries. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals who are located in the European Economic Area ("EEA"), and the processing of personal data that takes place in the EEA, is regulated by the GDPR, which went into effect in May 2018 and which imposes obligations on companies that operate in our industry with respect to the processing of personal data and the cross-border transfer of such data. The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and policies. If our or our partners' or service providers' privacy or data security measures fail to comply with the GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data and/or fines of up to 20 million Euros or up to 4% of the total worldwide annual turnover of the group of companies of the preceding financial year, whichever is higher, as well as compensation claims by affected individuals, negative publicity, reputational harm and a potential loss of business and goodwill.
The GDPR places restrictions on the cross-border transfer of personal data from the EU to countries that have not been found by the EC to offer adequate data protection legislation. There are ongoing concerns about the ability of companies to transfer personal data from the EU to other countries. In July 2020, the Court of Justice of the EU (the "CJEU") invalidated the EU-U.S. Privacy Shield, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the U.S. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for international transfers of personal data from the EEA. This CJEU decision resulted in increased scrutiny on data transfers and increased our costs of compliance with data privacy legislation as well as our costs of negotiating appropriate privacy and security agreements with our vendors and business partners.

In October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which serves as a replacement to the EU-U.S. Privacy Shield. The EC adopted the adequacy decision on July 10, 2023. The adequacy decision permits U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the EU to the U.S. However, some privacy advocacy groups have already suggested that they will be challenging the EU-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. The uncertainty around this issue has the potential to impact our business. Following the withdrawal of the UK from the EU, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the UK and includes parallel obligations to those set forth by GDPR. In relation to data transfers, both the UK and the EU have determined, through separate "adequacy" decisions, that data transfers between the two jurisdictions are in compliance with the UK Data Protection Act and the GDPR, respectively. The UK and the U.S. have also agreed to a U.S.-UK "Data Bridge", which functions similarly to the EU-U.S. Data Privacy Framework and provides an additional legal mechanism for companies to transfer data from the UK to the U.S. In addition to the UK, Switzerland is also in the process of approving an adequacy decision in relation to the Swiss-U.S. Data Privacy Framework (which would function similarly to the EU-U.S. Data Privacy Framework and the U.S.-UK Data Bridge in relation to data transfers from Switzerland to the U.S.). Any changes or updates to these developments have the potential to impact our business.

Beyond GDPR, there are privacy and data security laws in a growing number of countries around the world. While many loosely follow GDPR as a model, other laws contain different or conflicting provisions. These laws will impact our ability to conduct our business activities, including both our clinical trials and the sale and distribution of commercial products, through increased compliance costs, costs associated with contracting and potential enforcement actions.

While we continue to address the implications of the recent changes to data privacy regulations, data privacy remains an evolving landscape at both the domestic and international level, with new regulations coming into effect and continued legal challenges, and our efforts to comply with the evolving data protection rules may be unsuccessful. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. We must devote significant resources to understanding and complying with this changing landscape. Failure to comply with laws regarding data protection would expose us to risk of enforcement actions taken by data protection authorities in the EEA and elsewhere and carries with it the potential for significant penalties if we are found to be non-compliant. Similarly, failure to comply with federal and state laws in the U.S. regarding privacy and security of personal information could expose us to penalties under such laws. Any such failure to comply with data protection and privacy laws could result in government-imposed fines or orders requiring that we change our practices, claims for damages or other liabilities, regulatory investigations and enforcement action, litigation and significant costs for remediation, any of which could adversely affect our business. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects.

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

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, consultants, collaborators and vendors. Misconduct by these partners could include intentional, reckless and/or negligent conduct or unauthorized activities that violate FDA regulations or similar regulations of comparable foreign regulatory authorities; provide inaccurate information to the FDA or comparable foreign regulatory authorities; fail to comply with manufacturing standards, federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities; fail to comply with state drug pricing transparency filing requirements; fail to report financial information or data accurately; or fail to disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. This could include violations of HIPAA, other U.S. federal and state laws, and requirements of foreign jurisdictions, including the GDPR. We are also exposed to risks in connection with any insider trading violations by employees or others affiliated with us. It is not always possible to identify and deter employee or third-party misconduct, and the precautions we take to detect and prevent these activities may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from significant penalties, governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards, regulations, guidance or codes of conduct. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

***If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.***

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations and the operations of our third-party vendors also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

***Laws and regulations governing international operations we may have in the future may preclude us from developing, manufacturing and selling certain products outside of the U.S. and require us to develop and implement costly compliance programs.***

We are subject to numerous laws and regulations in each jurisdiction outside of the U.S. in which we operate. The creation, implementation and maintenance of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

The FCPA prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the U.S. to comply with certain accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls. The FCPA is enforced by the DOJ and the SEC.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals, clinics, universities and similar institutions are operated by the government, and doctors and other healthcare professionals are considered

foreign officials. Certain payments to healthcare professionals in connection with clinical trials, regulatory approvals, sales and marketing, and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions. Because the FCPA applies to indirect payments, the use of third parties and other collaborators can increase potential FCPA risk, as we could be held liable for the acts of third parties that do not comply with the FCPA's requirements.

The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

Like the FCPA, the UK Bribery Act and other anti-corruption laws throughout the world similarly prohibit offers and payments made to obtain improper business advantages, including offers or payments to healthcare professionals and other government and non-government officials. These other anti-corruption laws also can result in substantial financial penalties and other collateral consequences.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the U.S., or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Our expansion outside of the U.S., has required, and will continue to require, us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain drugs and product candidates outside of the U.S., which could limit our growth potential and increase our development costs.

***With the passage of the CREATES Act, we are exposed to possible litigation and damages by competitors who may claim that we are not providing sufficient quantities of our approved products on commercially reasonable, market-based terms for testing in support of their ANDAs and 505(b)(2) applications.***

In December 2019, former President Trump signed legislation intended to facilitate the development of generic and biosimilar products. The bill, previously known as the CREATES Act, authorizes sponsors of abbreviated new drug applications ("ANDAs") and 505(b)(2) applications to file lawsuits against companies holding NDAs that decline to provide sufficient quantities of an approved reference drug on commercially reasonable, market-based terms. Drug products on the FDA's drug shortage list are exempt from these new provisions unless the product has been on the list for more than six continuous months or the FDA determines that the supply of the product will help alleviate or prevent a shortage.

To bring an action under the statute, an ANDA or 505(b)(2) sponsor must take certain steps to request the reference product, which, in the case of products covered by a REMS with elements to assure safe use, include obtaining authorization from the FDA for the acquisition of the reference product. If the sponsor does bring an action for failure to provide a reference product, there are certain affirmative defenses available to the NDA holder, which must be shown by a preponderance of evidence. If the sponsor prevails in litigation, it is entitled to a court order directing the NDA holder to provide, without delay, sufficient quantities of the applicable product on commercially reasonable, market-based terms, plus reasonable attorney fees and costs.

Additionally, the new statutory provisions authorize a federal court to award the product developer an amount "sufficient to deter" the NDA holder from refusing to provide sufficient product quantities on commercially reasonable, market-based terms if the court finds, by a preponderance of the evidence, that the NDA holder did not have a legitimate business justification to delay providing the product or failed to comply with the court's order. For the purposes of the statute, the term "commercially reasonable, market-based terms" is defined as (1) the nondiscriminatory price at or below the most recent wholesale acquisition cost for the product, (2) a delivery schedule that meets the statutorily defined timetable, and (3) no additional conditions on the sale.

Although we intend to comply fully with the terms of these statutory provisions, we are still exposed to potential litigation and damages by competitors who may claim that we are not providing sufficient quantities of our approved products on commercially reasonable, market-based terms for testing in support of ANDAs and 505(b)(2) applications. Such litigation would subject us to additional litigation costs, damages and reputational harm, which could lead to lower revenues. The CREATES Act may enable generic competition with XPOVIO and any of our product candidates, if approved, which could impact our ability to maximize product revenue. In September 2022, the FDA issued draft guidance outlining certain of the provisions under this statute.

***We are subject to governmental export and import controls that could impair our or our collaborators' ability to compete in international markets due to licensing requirements and subject us or them to liability if we or they are not in compliance with applicable laws.***

Our products are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls. Exports of our products outside of the U.S. must be made in compliance with these laws and regulations. If we or our collaborators fail to comply with these laws and regulations, we or they and certain of our or their employees could be subject to substantial civil or criminal penalties, including the possible loss of export or import privileges; fines, which may be imposed on us or our collaborators and the respective responsible employees or managers; and, in extreme cases, the incarceration of responsible employees or managers.

In addition, changes in our products or changes in applicable export or import laws and regulations may create delays in the introduction, provision, or sale of our products in international markets, prevent customers from using our products or, in some cases, prevent the export or import of our products to certain countries, governments or persons altogether. Any limitation on our ability to export, provide, or sell our products could adversely affect our business, financial condition and results of operations.

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

***We have incurred significant losses since inception, expect to continue to incur significant losses, and may never achieve or maintain profitability.***

Since inception, we have incurred significant operating losses. Our net loss was $37.4 million for the quarter ended March 31, 2024. As of March 31, 2024, we had an accumulated deficit of $1.5 billion. Although we received our first FDA-approval for XPOVIO in July 2019, we may never attain profitability or positive cash flows from operations. We have historically financed our operations principally through product sales, private placements of our common stock, proceeds from our initial public offering and follow-on offerings of common stock, proceeds from the issuance of convertible debt, proceeds from a revenue interest financing agreement, proceeds from sales of common stock under our "at the market offering" program and cash generated from our business development activities. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs, the pursuit of regulatory approvals within and outside of the U.S., and the commercialization of XPOVIO. We expect to continue to incur significant expenses and operating losses as we continue to commercialize XPOVIO in the U.S. and engage in activities to prepare for the potential approval and commercialization of additional indications for selinexor as well as any other product candidates we develop or acquire. The net losses we incur may fluctuate significantly from quarter to quarter.

While we began to generate revenue from the sales of XPOVIO in July 2019 and have received revenue from our license arrangements, such as the partnership we have with Antengene Therapeutics Limited ("Antengene") for our programs across most of the Asia-Pacific region, and with Menarini for our programs in Europe, Latin America, certain Middle East and Africa regions and other key countries, there can be no assurance as to the amount or timing of future product or license and other revenues, and we may not achieve profitability for several years, if at all. Our ability to become and remain profitable depends significantly on our success in many areas, including:

- effectively commercializing XPOVIO or any future products either on our own or with a collaborator, including by maintaining a full commercial organization required to market, sell and distribute our products, and achieving an adequate level of market acceptance;
- the impact of current or future competing products on product sales of XPOVIO or any of our future products;
- obtaining sufficient pricing, coverage and reimbursement, including government pricing and reimbursement policies or a change in the mix of our business effecting rebates related to 340B Programs, Medicare and Medicaid, for XPOVIO and any of our other approved products from private and government payers and the impact of any pricing changes, any of which can impact our gross-to-net provisions related to product sales;
- initiating and successfully completing clinical trials required to file for, obtain and maintain marketing approval for our product candidates;
- obtaining and maintaining regulatory approvals, either by us or our collaborators, and the timing of such approvals;
- manufacturing at commercial scale;
- establishing and managing any collaborations for the development, marketing and/or commercialization of our products and product candidates, including the level of success of our collaborators' efforts and the timing and amount of any milestone or royalty payments we may receive;

- obtaining, maintaining and protecting our intellectual property rights;
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage or as co-pay amounts under third-party coverage; for example, multiple myeloma foundation closures during 2023 resulted in significantly increased use of our PAP, which adversely impacted our 2023 revenues; and
- navigating the negative impacts to healthcare systems, the ability of our clinical trial sites to conduct current or future trials and the regulatory review process as the result of pandemics or other public health emergencies.

We anticipate that our operating expenses will continue to be significant and increase as we continue to:

- commercialize XPOVIO in the U.S., including maintaining our commercial infrastructure;
- obtain and/or maintain regulatory approval for XPOVIO and our product candidates, including completing any required post-marketing requirements to the satisfaction of the FDA or other regulatory agencies;
- expand our research and development programs, identify additional product candidates and initiate and conduct clinical trials, including clinical trials required by the FDA or other regulatory agencies in addition to those that have been or are currently expected to be conducted;
- maintain, expand and protect our intellectual property portfolio;
- manufacture XPOVIO and our product candidates; and
- acquire or in-license other products, product candidates or technologies.

Because of the numerous risks and uncertainties associated with pharmaceutical product development and commercialization, we are unable to accurately predict the timing or amount of our revenue and expenses or when, or if, we will be able to achieve profitability. We cannot be certain that our revenue from sales of XPOVIO alone, in the currently approved indications, will be sufficient for us to become profitable for several years, if at all. We may never generate revenues that are significant or large enough to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development and commercialization efforts, expand our business and/or continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

***We will need additional funding to achieve our business objectives. If we are unable to raise capital when needed or on acceptable terms, we would be forced to delay, reduce or eliminate our research and development programs and/or commercialization efforts.***

Discovering, developing and commercializing products involve time-consuming, expensive and uncertain processes that take years to complete. We have used substantial funds to develop XPOVIO and expect our operating expenses to continue to increase as we continue to commercialize XPOVIO or any future approved product, conduct further research and development of our product candidates, seek marketing approval and prepare for commercialization of selinexor in additional indications or for our other product candidates, if approved, to the extent that such functions are not the responsibility of a collaborator. Furthermore, we will continue to incur additional costs associated with operating as a public company, hiring additional personnel and expanding our geographical reach. Although currently XPOVIO is commercially available in three indications, we do not anticipate that our revenue from product sales of XPOVIO or any funds we may receive from our collaborators will be sufficient for us to become profitable for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives.

As of March 31, 2024, we believe that our existing cash, cash equivalents and investments will enable us to fund our current operating and capital expenditure plans for at least twelve months from the date of issuance of the financial statements contained in this Quarterly Report on Form 10-Q. The amount and timing of our future capital requirements will depend on many factors, including, but not limited to:

- the scope, progress, results, timing and costs of our current and planned development efforts and regulatory review of our product candidates;
- the amount and timing of revenues from sales of XPOVIO, or any product candidate that we develop or acquire;
- the cost of, and our ability to expand and maintain, the commercial infrastructure required to support the commercialization of XPOVIO and any other product for which we receive marketing approval, including medical affairs, manufacturing, marketing and distribution functions;

- our ability to establish and maintain collaboration, partnership, licensing, marketing, distribution or other arrangements on favorable terms and the level and timing of success of these arrangements, and our ability to use proceeds of those arrangements in our business as opposed to being required to pay those proceeds to the lenders of our $100.0 million senior secured term loan facility (the "Term Loan") and/or holders of the Convertible Senior Notes due 2025 (the "2025 Notes") and the secured Convertible Senior Notes due 2029 (the "2029 Notes");
- the extent to which we acquire or in-license other products, product candidates and technologies, and our ability to enter into such acquisitions and in-licenses pursuant to the restrictions under the Term Loan and the 2029 Notes; and
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims.

In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders. If we raise additional funds by issuing equity securities, dilution to our existing stockholders will result. In addition, as a condition to providing additional funding to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Moreover, in addition to the restrictions and prohibitions in respect of the Term Loan and the 2029 Notes, the restrictions and prohibitions contained in the Amended Revenue Interest Agreement (defined below) and the repayment requirements in respect of such obligations from proceeds of such transactions, any future debt financing, if available and permitted, may involve further restrictive covenants that could limit our flexibility in conducting future business activities and using transaction proceeds in our business and, in the event of insolvency, the Term Loan, the 2029 Notes, the 2025 Notes, the Amended Revenue Interest Agreement obligations, and any further indebtedness, if available and permitted, would be paid before holders of equity securities received any distribution of corporate assets. Our ability to satisfy and meet our current and any future debt service obligations will depend upon our future performance, which will be subject to financial, business and other factors affecting our operations, many of which are beyond our control.

Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital due to favorable market conditions or strategic considerations. Any future fundraising efforts could divert our management's attention away from their day-to-day activities. Further, adequate additional financing may not be available to us on acceptable terms, or at all. In addition, raising funds in the current economic environment may present additional challenges. For example, any sustained disruption in the capital markets from adverse macroeconomic conditions, such as the disruption and uncertainty caused by inflation, sustained high interest rates and slower economic growth or recession, could negatively impact our ability to raise capital and we cannot predict the extent or duration of such macro-economic disruptions. Moreover, there has been recent turmoil in the global banking system, which could result in a situation where we lose our deposits, or access to our deposits, and are unable to obtain financing from other sources. If adequate funds are not available to us on a timely basis or on attractive terms, we may be required to delay, reduce or eliminate our research and development programs or any current or future commercialization efforts for one or more of our products or product candidates, any of which could have a material adverse effect on our business, operating results and prospects.

***Our Revenue Interest Agreement with HCRx, as amended, contains various covenants and other provisions, which, if violated, could, subject to an intercreditor agreement among HCRx, the Term Loan lenders, and the holders of the 2029 Notes, result in the acceleration of payments due under such agreement or the foreclosure on the pledged collateral, including all of our present and future assets relating to selinexor.***

In September 2019, we entered into the Revenue Interest Financing Agreement (the "Revenue Interest Agreement") with HealthCare Royalty Partners III, L.P. and HealthCare Royalty Partners IV, L.P. ("HCRx") and which was amended in June 2021, August 2023 and May 2024 (the "Amended Revenue Interest Agreement"). Pursuant to the Amended Revenue Interest Agreement, we are required to comply with various covenants relating to the conduct of our business and the commercialization of XPOVIO, including obligations to use commercially reasonable efforts to commercialize our products. In addition, the Amended Revenue Interest Agreement limits our ability to incur or prepay indebtedness, create or incur liens, pay dividends on or repurchase outstanding shares of our capital stock or dispose of assets. The Amended Revenue Interest Agreement also includes customary events of default upon the occurrence of enumerated events, including non-payment of revenue interests, failure to perform certain covenants and the occurrence of insolvency proceedings, specified judgments, specified cross-defaults or specified revocations, or withdrawals or cancellations of regulatory approval for XPOVIO. Upon the occurrence of an event of default and in the event of a change of control, HCRx may accelerate payments due under the Amended Revenue Interest Agreement up to $128.3 million, less the aggregate of all of the payments paid to HCRx after the date of the May 2024 amendment. Our obligations to HCRx are secured by a second-priority security interest in certain assets of ours related to selinexor, which shares such second priority with the 2029 Notes and which is subordinate to the first-priority security interest securing the Term Loan. Subject to an intercreditor agreement with the Term Loan lenders and the holders of the 2029 Notes, in the event of an uncured default by us under the Amended Revenue Interest Agreement results in an acceleration of obligations by HCRx which we are unable to pay, HCRx may be able to foreclose on the collateral that was pledged to HCRx. Any such foreclosure remedy would significantly and adversely affect us and could result in us losing our interest in such assets, which would have an adverse material impact on our business.

***Our new Credit Agreement and Indenture related to the 2029 Notes contains various covenants and other provisions, which will limit the manner in which we may operate, and, if violated, could, subject to an intercreditor agreement among HCRx, the Term Loan lenders, and the holders of the 2029 Notes, result in the acceleration of payments due under such agreements or the foreclosure on the pledged collateral, including all of our present and future assets.***

The May 2024 credit and guaranty agreement (the "Credit Agreement") and indenture governing the 2029 Notes (the "Indenture") contain, and any future indebtedness that we incur may contain, various negative covenants that restrict, among other things, our indebtedness, liens, fundamental changes, asset sales, investments and other matters. In addition, the Credit Agreement and the Indenture each have a financial covenant requiring us to maintain liquidity of at least $25.0 million at all times. As a result, we are limited in the manner in which we conduct our business and we may be unable to engage in favorable business activities. The Credit Agreement and Indenture also contain certain events of default, after which the Term Loan or the 2029 Notes may be due and payable immediately, including, without limitation, withdrawal of approval of certain indications of selinexor, payment defaults, material inaccuracy of representations and warranties, covenant defaults, bankruptcy and insolvency proceedings, cross-defaults to certain other agreements, judgments against us and our subsidiaries, change in control and lien priority. Our obligations under the Credit Agreement and the Indenture are secured by substantially all of our assets. Subject to an intercreditor agreement with HCRx, the Term Loan lenders and the holders of the 2029 Notes, if we are unable to pay our obligations after acceleration of the Term Loan or the 2029 Notes and the lenders under the Term Loan or holders of the 2029 Notes foreclose on our assets, it would significantly and adversely affect us and could result in us losing our interest in such assets, which would have an adverse material impact on our business.

***Our indebtedness could limit cash flow available for our operations, expose us to risks that could adversely affect our business, financial condition and results of operations and impair our ability to satisfy our obligations under the Term Loan, the 2029 Notes, the 2025 Notes or the Amended Revenue Interest Agreement.***

We have incurred (i) $172.5 million of indebtedness as a result of the sale of the 2025 Notes, of which $24.5 million will remain outstanding following completion of the May 2024 exchange of certain of our 2025 Notes for 2029 Notes (the "Exchange Transactions"); (ii) $263.3 million of indebtedness under the Amended Revenue Interest Agreement, of which $135.0 million will have been repaid after giving effect to the May 2024 amendment to the Amended Revenue Interest Agreement, resulting in a remaining maximum aggregate repayment amount to HCRx of $128.3 million, (iii) $100.0 million of indebtedness under the Term Loan, and (iv) $116.0 million of indebtedness that will be issued as a result of the issuance of the 2029 Notes pursuant to the Exchange Transactions. We may also incur additional indebtedness to meet future financing needs, to the extent such indebtedness is available and permitted. Our indebtedness could have significant negative consequences for our security holders and our business, results of operations and financial condition by, among other things:

- increasing our vulnerability to adverse economic and industry conditions;
- limiting our ability to obtain additional financing;
- requiring the dedication of a substantial portion of our cash flow from operations to service our indebtedness, which would reduce the amount of cash available for other purposes;
- limiting our flexibility to plan for, or react to, changes in our business;
- diluting the interests of our existing stockholders as a result of issuing shares of our common stock upon conversion of the 2029 Notes or the 2025 Notes; and
- placing us at a possible competitive disadvantage with competitors that are less leveraged than us or have better access to capital.

Our ability to pay the principal of or interest or other obligations on our present and any future indebtedness, including our remaining obligations to HCRx, or to make cash payments in connection with any conversion of the 2029 Notes or the 2025 Notes depends on our future performance, which is subject, in part, to economic, financial, competitive and other factors beyond our control. Our business may not generate cash flow from operations in the future sufficient to service the Term Loan, the Amended Revenue Interest Agreement, the 2029 Notes, the 2025 Notes or any other future indebtedness and make necessary capital expenditures.

***We may not have the ability to raise the funds necessary to settle any conversions of or other obligations in respect of the 2029 Notes or the 2025 Notes required to be settled in cash, to repurchase the 2029 Notes or the 2025 Notes for cash upon a fundamental change, to pay the redemption price for any 2029 Notes or 2025 Notes we redeem or to refinance the 2029 Notes or the 2025 Notes, and any future debt we incur may contain limitations on our ability to pay cash upon conversion or repurchase of the 2029 Notes or the 2025 Notes.***

Holders may require us to repurchase their 2029 Notes or 2025 Notes following a fundamental change at a cash repurchase price generally equal to the principal amount of the 2029 Notes or the 2025 Notes to be repurchased, plus accrued and unpaid interest. In addition, upon conversion, with respect to the 2025 Notes, unless we elect to deliver solely shares of our common stock to settle conversions (other than paying cash in lieu of delivering any fractional share), we must satisfy the conversion in cash. If we do not have enough available cash at the time we are required to repurchase the 2029 Notes or the 2025 Notes, pay cash amounts due upon conversion or redemption of or otherwise required to be paid in respect of the 2029 Notes or the 2025 Notes or refinance the 2029 Notes or the 2025 Notes, we may be required to adopt one or more alternatives, such as selling assets, restructuring indebtedness or obtaining additional debt financing or equity capital on terms that may be onerous or highly dilutive. Our ability to refinance the 2029 Notes or the 2025 Notes or other future indebtedness will depend on the capital markets, our financial condition at such time and our obligations under any other existing indebtedness in effect at such time. We may not be able to engage in any of these activities on desirable terms, or at all, which could result in a default on our debt obligations, including the 2029 Notes and the 2025 Notes. In addition, our ability to repurchase the 2029 Notes or the 2025 Notes, to pay cash upon conversion or redemption of the 2029 Notes or the 2025 Notes or to refinance the 2029 Notes or the 2025 Notes may be limited by law, regulatory authority or agreements governing any future indebtedness that we may incur. Our failure to repurchase the 2029 Notes or the 2025 Notes at a time when the repurchase is required by the Indenture or to pay cash upon conversion of or in respect of other obligations under the 2029 Notes or the 2025 Notes as required by the Indenture would constitute a default under the Indenture. A default under the Indenture or the fundamental change itself could also lead to a default under agreements governing our future indebtedness, if any. Moreover, the occurrence of a fundamental change under the Indenture could constitute an event of default under any such agreements. If the repayment of the related indebtedness were to be accelerated after any applicable notice or grace periods, we may not have sufficient funds to repay the indebtedness and repurchase the 2029 Notes or the 2025 Notes or to pay cash upon conversion of the 2029 Notes or the 2025 Notes.

***The conditional conversion feature of the 2025 Notes, if triggered, may adversely affect our financial condition and operating results.***

In the event the conditional conversion feature of the 2025 Notes is triggered, holders of Notes will be entitled to convert the 2025 Notes at any time during specified periods at their option. If one or more holders elect to convert their Notes, unless we elect to satisfy our conversion obligation by delivering solely shares of our common stock (other than paying cash in lieu of delivering any fractional share), we would be required to settle a portion or all of our conversion obligation in cash, which could adversely affect our liquidity. In addition, even if holders do not elect to convert their Notes, we could be required under applicable accounting rules to reclassify all or a portion of the outstanding principal amount of the 2025 Notes as a current rather than long-term liability, which would result in a material reduction of our net working capital.

***The accounting method for convertible debt securities such as the 2025 Notes and the 2029 Notes could have a material effect on our reported financial results.***

Conversions of the 2025 Notes may be settled in cash or shares, or a combination of cash and shares. Conversions of the 2029 Notes will be settled in shares. Under the if-converted method, the maximum potential dilutive impact of the conversion of the 2025 Notes or the 2029 Notes is assumed when calculating diluted earnings per share during periods of net income. This could result in a material impact to diluted earnings per share. Diluted earnings per share is not impacted by the 2025 Notes or the 2029 Notes during periods of net loss.

***Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our product candidates.***

Until such time, if ever, as we can generate substantial revenues from the sale of our products, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and/or licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of common stockholders. In addition, our ability to raise additional capital through the sale of equity or convertible debt securities may be limited by the extent of our then remaining authorized and available shares of Common Stock. Debt financing, if available and permitted, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring

dividends. For example, during the term of the Amended Revenue Interest Agreement, we cannot make any voluntary or optional cash payment or prepayment on our existing convertible debt and cannot enter into any new debt without the consent of HCRx.

If we raise additional funds through further collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our research and drug development or current or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

***Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.***

Global credit and financial markets have experienced extreme disruptions over the past several years. Such disruptions have resulted, and could in the future result, in diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. Our general business strategy may be compromised by economic downturns, a volatile business environment and unpredictable and unstable market conditions, such as the current global situation resulting, in part, from the ongoing conflict between Russia and Ukraine, the war between Israel and Hamas, inflation, failures and instability in U.S. and international banking systems, sustained high interest rates and slower economic growth or recession. If the equity and credit markets deteriorate, it may make any necessary equity or debt financing more difficult to secure, more costly or more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could harm our growth strategy, financial performance and stock price and could require us to delay or abandon plans with respect to our business, including clinical development plans. Further, recent developments in the banking industry could adversely affect our business. If the financial institutions with which we do business enter receivership or become insolvent in the future, there is no guarantee that the Department of the Treasury, the Federal Reserve and the FDIC will intercede to provide us and other depositors with access to balances in excess of the $250,000 FDIC insurance limit, that we would be able to access our existing cash, cash equivalents and investments, that we would be able to maintain any required letters of credit or other credit support arrangements, or that we would be able to adequately fund our business for a prolonged period of time or at all, any of which could have a material adverse effect on our business, financial condition and results of operations. We cannot predict the impact that the high market volatility and instability of the banking sector more broadly could have on economic activity and our business in particular. In addition, there is a risk that one or more of our current service providers, manufacturers or other third parties with which we conduct business may not survive difficult economic times, including the current global situation resulting, in part, from the ongoing conflict between Russia and Ukraine, the war between Israel and Hamas, the instability of the banking sector, and the uncertainty associated with current worldwide economic conditions, which could directly affect our ability to attain our operating goals on schedule and on budget.

**Risks Related to Our Dependence on Third Parties**

***We depend on collaborations with third parties for certain aspects of the development, marketing and/or commercialization of XPOVIO and/or our product candidates. If those collaborations are not successful, or if we are not able to maintain our existing collaborations or establish additional collaborations, we may have to alter our development and commercialization plans and may not be able to capitalize on the market potential of XPOVIO or our product candidates, if approved.***

Our drug development programs and the commercialization of our products and product candidates, if approved, require local expertise and substantial additional cash to fund expenses. We expect to maintain our existing collaborations and collaborate with additional pharmaceutical and biotechnology companies for certain aspects of the development, marketing and/or commercialization of our products and product candidates. For example, we are parties to license arrangements with Antengene and Menarini and distribution agreements with Promedico Ltd. and FORUS Therapeutics Inc. for the development, marketing and/or commercialization of selinexor in certain geographies outside of the U.S., and we expect to rely on additional partners to develop and commercialize our products outside of the U.S. In addition, we intend to seek one or more collaborators to aid in the further development, marketing and/or commercialization of selinexor and our other compounds for indications both within and outside of oncology. All of the risks relating to product development, regulatory approval and commercialization described in this Quarterly Report on Form 10-Q also apply to the activities, including activities in any country or territory outside of the U.S. and EU, as applicable, of our collaborators.
Potential collaborators include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies and we face significant competition in seeking appropriate collaborators, including as a result of a significant number of recent business combinations among large pharmaceutical companies that have reduced the number of potential collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon the assessment of the potential collaborator's expertise, its current and expected resources and competing priorities, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or foreign regulatory authorities, the potential market for the product or product candidate, the costs and complexities of manufacturing and delivering such product or product candidate to patients, the

potential of competing products, the existence of uncertainty with respect to our ownership of intellectual property, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. A potential collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us.

Collaborations are complex and time-consuming to negotiate, document and manage. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all, or we may be restricted under then-existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. If we are unable to maintain our current collaboration agreements or enter into new collaboration agreements, we may have to curtail, reduce or delay the development or commercialization programs for our products or product candidates, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements, and our collaboration agreements may not lead to the development or commercialization of our products or product candidates in the most efficient manner, or at all, and may result in lower product revenues or profitability to us than if we were to market and sell these products ourselves. In connection with any such arrangements with third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development, marketing and/or commercialization of our products or product candidates. Further, if our collaborations do not result in the successful development and commercialization of our products or product candidates or if any one of our collaborators terminates its agreement with us, we may not receive any future milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, the development and commercialization of our products or product candidates could be delayed and we may need additional resources to develop product candidates.
Collaborations involving our products and product candidates pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected or in compliance with applicable local and national laws and regulatory requirements;
- collaborators may not pursue development, marketing and/or commercialization of our products or product candidates or may elect not to continue or renew development, marketing or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- a collaborator with marketing and distribution rights to one or more products or product candidates may not commit sufficient resources to the marketing and distribution of our products or product candidates;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development or commercialization, might cause delays or termination of the research, development or commercialization of products or product candidates, might lead to additional responsibilities for us with respect to our products or product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;

- we may lose certain valuable rights under circumstances identified in any collaboration arrangement that we enter into, such as if we undergo a change of control;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development, marketing and/or commercialization of the applicable products or product candidates or to enter into new collaboration agreements;
- collaborators may learn about our discoveries and use this knowledge to compete with us in the future; and
- the number and type of our collaborations could adversely affect our attractiveness to other collaborators or acquirers.

If any of these events occurs, the market potential of our products and product candidates, if approved, could be reduced, and our business could be materially harmed.

***If we are unable to establish and maintain our agreements with third parties to distribute XPOVIO to patients, our results of operations and business could be adversely affected.***

We rely on third parties to commercially distribute XPOVIO to patients. For example, we have contracted with a limited number of specialty pharmacies, which sell XPOVIO directly to patients, and specialty distributors, which sell XPOVIO to healthcare entities who then resell XPOVIO to patients. While we have entered into agreements with each of these pharmacies and distributors to distribute XPOVIO in the U.S., they may not perform as agreed or they may terminate their agreements with us. We may also need to enter into agreements with additional pharmacies or distributors, and there is no guarantee that we will be able to do so on a timely basis, at commercially reasonable terms, or at all. If we are unable to maintain and, if needed, expand, our network of specialty pharmacies and specialty distributors, we would be exposed to substantial distribution risk.
The use of specialty pharmacies and specialty distributors involves certain risks, including, but not limited to, risks that these organizations will:

- not provide us accurate or timely information regarding their inventories, the number of patients who are using XPOVIO or serious adverse reactions, events and/or product complaints regarding XPOVIO;
- not effectively sell or support XPOVIO or communicate publicly concerning XPOVIO in a manner that is contrary to FDA rules and regulations;
- reduce their efforts or discontinue to sell or support, or otherwise not effectively sell or support, XPOVIO;
- not devote the resources necessary to sell XPOVIO in the volumes and within the time frames that we expect;
- be unable to satisfy financial obligations to us or others; or
- cease operations.

Any such events may result in decreased product sales, which would harm our results of operations and business.

***We rely on third parties as we conduct our clinical trials and some aspects of our research and preclinical studies, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing.***

We rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, as we conduct our clinical trials. We currently rely and expect to continue to rely on third parties to conduct some aspects of our research and preclinical studies. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our drug development activities.

Our reliance on these third parties for research and development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with GCP standards when conducting, recording and reporting the results of clinical trials to ensure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The EMA also requires us to comply with comparable standards. Regulatory authorities ensure compliance with these requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of the third parties that we rely on in connection with our clinical trials fail to comply with applicable requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or other comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with such requirements. We also are required to register ongoing clinical trials and post the results of

completed clinical trials on a government-sponsored database, such as ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our products. In such an event, our financial results and the commercial prospects for our products or product candidates, if approved, could be harmed, our costs could increase and our ability to generate revenues could be delayed, impaired or foreclosed.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of such third parties could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

***We rely on third parties to conduct investigator-sponsored clinical trials of selinexor and our other product candidates. Any failure by a third party to meet its obligations with respect to the clinical development of our product candidates may delay or impair our ability to obtain regulatory approval for selinexor and our other product candidates.***

We rely on academic and private non-academic institutions to conduct and sponsor clinical trials relating to selinexor and our other product candidates. We do not solely control the design or conduct of the investigator-sponsored trials, and it is possible that the FDA or foreign regulatory authorities will not view these investigator-sponsored trials as providing adequate support for future clinical trials, whether controlled by us or third parties, for any one or more reasons, including elements of the design, execution of the trials, safety concerns or other trial results.

Such arrangements will provide us certain information rights with respect to the investigator-sponsored trials, such as access to and the ability to use and reference the data, including for our own regulatory filings, resulting from the investigator-sponsored trials. However, we do not have control over the timing and reporting of the data from investigator-sponsored trials, nor do we own the data from the investigator-sponsored trials. If we are unable to confirm or replicate the results from the investigator-sponsored trials or if negative results are obtained, we would likely be further delayed or prevented from advancing clinical development of our product candidates. Further, if investigators or institutions breach their obligations with respect to the clinical development of our product candidates, or if the data proves to be inadequate compared to the first-hand knowledge we might have gained had the investigator-sponsored trials been sponsored and conducted by us, then our ability to design and conduct any future clinical trials ourselves may be adversely affected.

Additionally, the FDA or foreign regulatory authorities may disagree with the sufficiency of our right to reference the preclinical, manufacturing or clinical data generated by these investigator-sponsored trials, or our interpretation of preclinical, manufacturing or clinical data from these investigator-sponsored trials. If so, the FDA or foreign regulatory authorities may require us to obtain and submit additional preclinical, manufacturing, or clinical data before we may initiate our planned trials and/or may not accept such additional data as adequate to initiate our planned trials.

***We are completely dependent on third parties for the manufacture of our products and product candidates and any difficulties, disruptions, delays or unexpected costs, or the need to find alternative sources, could adversely affect our results of operations, profitability and future business prospects.***

We do not own or operate, and currently have no plans to establish, any manufacturing facilities for our products or product candidates. We currently rely, and expect to continue to rely, on third-party contract manufacturers to manufacture our products and product candidates for our commercial and clinical use.

Facilities used by our third-party manufacturers may be inspected by the FDA after we submit a marketing application and before potential approval of the product candidate and are also subject to ongoing periodic unannounced inspections by the FDA for compliance with cGMP and other regulatory requirements following approval. Similar regulations apply to manufacturers of our product candidates for use or sale in foreign countries. We do not control the manufacturing processes of, and are completely dependent on, our third-party manufacturers for compliance with the applicable regulatory requirements for the manufacture of our products and product candidates. Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the U.S. If our manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA and any applicable foreign regulatory authority, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. If these facilities are not approved for commercial manufacture or are not able to maintain approval, we may need to find alternative manufacturing facilities, which could significantly impact our ability to develop, obtain regulatory approval for or market our products or product candidates as alternative qualified manufacturing facilities may not be available on a timely or cost-efficient basis, or at all. Failure by any of our manufacturers to comply with

applicable cGMP regulations or other regulatory requirements could result in sanctions being imposed on us or the contract manufacturer, including fines, injunctions, civil penalties, delays, suspensions or withdrawals of approvals, operating restrictions, interruptions in supply and criminal prosecutions, any of which could significantly and adversely affect supplies of our products or product candidates and have a material adverse impact on our business, financial condition and results of operations.

The clinical and commercial supplies of the drug product for XPOVIO are currently manufactured pursuant to a combination of long-term supply agreements and as-needed purchase order agreements with our third-party manufacturers. Our ability to have our products manufactured in sufficient quantities and at acceptable costs to meet our commercial demand and clinical development needs is dependent on the uninterrupted and efficient operation of our third-party contract manufacturers' facilities. Further, through our third-party contract manufacturers and data service providers, we provide serialized commercial products as required to comply with the DSCSA and its foreign equivalents where applicable. If our third-party contract manufacturers or data service providers fail to support our efforts to continue to serialize, track, trace and authenticate units of our products in compliance with these requirements and their and their foreign equivalents, as well as any future requirements, we may face legal penalties or be restricted from selling our products.

Reliance on third-party manufacturers entails other risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach, termination or nonrenewal of a manufacturing agreement by the third party, including at a time that is costly or inconvenient to us;
- the possible failure of the third party to manufacture our products or product candidates according to our schedule, or at all, including if the third-party manufacturer gives greater priority to the supply of other products over our products and product candidates, or otherwise does not satisfactorily perform according to the terms of the manufacturing agreement;
- equipment malfunctions, power outages or other general disruptions experienced by our third-party manufacturers to their respective operations and other general problems with a multi-step manufacturing process; and
- the possible misappropriation or disclosure by the third party or others of our proprietary information, including our trade secrets and know-how.

We currently rely on a single source supplier for our active pharmaceutical ingredient and our drug product manufacturing requirements. Any performance failure on the part of our existing or future manufacturers could delay clinical development, marketing approval or commercialization of our products or product candidates. If our suppliers or contract manufacturers are so affected, our supply chain could be disrupted, our product shipments could be delayed, our costs could be increased and our business could be adversely affected. If our current contract manufacturers cannot perform as agreed, we may be required to replace those manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our products and product candidates, we could incur added costs and delays in identifying and qualifying any such replacement. Consequently, we may not be able to reach agreement with third-party manufacturers on satisfactory terms, which could negatively impact our XPOVIO revenues or delay commercialization of any product candidates that are subsequently approved.
If, because of the factors discussed above, we are unable to have our products manufactured on a timely or sufficient basis, we may not be able to meet clinical development needs or commercial demand for our products or product candidates or we may not be able to manufacture our products in a cost-effective manner. As a result, we may lose sales, fail to generate projected revenues or suffer development or regulatory setbacks, any of which could have an adverse impact on our profitability and future business prospects.

**Risks Related to Our Intellectual Property**

***If we are unable to obtain and maintain patent protection for our products or product candidates and other discoveries, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize drugs and other discoveries similar or identical to ours, and our ability to successfully commercialize our products or product candidates and other discoveries may be adversely affected.***

Our success depends in large part on our ability to obtain and maintain patent protection in the U.S. and other countries with respect to our proprietary products and product candidates and other discoveries. We seek to protect our proprietary position by filing patent applications in the U.S. and abroad related to our novel products and product candidates and other discoveries that are important to our business. As of May 3, 2024, 171 patents were in force that relate to exportin 1 inhibitors, including composition of matter patents for selinexor, verdinexor and eltanexor in the U.S., and their use in targeted therapeutics. In addition, 32 patents were in force that relate to our PAK4/NAMPT inhibitors, including three composition of matter patents for KPT-9274 in the U.S. and its use in targeted therapeutics. With respect to our KPT-1200 program, as of May 3, 2024, 12 patents were in force that relate to IL-12

compositions and uses of IL-12 in targeted therapeutics. We cannot be certain that any other patents will issue with claims that cover any of our key products, product candidates or other discoveries.

The patent prosecution 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, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our product candidates or other discoveries, or which effectively prevent others from commercializing competitive drugs and discoveries. 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. For example, in some foreign jurisdictions, our ability to secure patents based on our filings in the U.S. may depend, in part, on our ability to timely obtain assignment of rights to the invention from the employees and consultants who invented the technology. 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. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

Assuming the other requirements for patentability are met, prior to March 2013, in the U.S., the first to invent the claimed invention was entitled to the patent, while outside of the U.S., the first to file a patent application is entitled to the patent. In March 2013, the U.S. transitioned to a first-inventor-to-file system in which, assuming the other requirements for patentability are met, the first inventor to file a patent application is entitled to the patent. We may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office (“USPTO”) or become involved in opposition, derivation, revocation, reexamination, or post-grant or inter partes review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our discoveries or drugs and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative discoveries or drugs in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the U.S. and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical discoveries and drugs, or limit the duration of the patent protection of our products, product candidates and discoveries. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing drugs similar or identical to ours.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time-consuming and unsuccessful.

Competitors or commercial supply companies or others may infringe our patents and other intellectual property rights. For example, we are aware of third parties selling a version of our lead product candidate for research purposes, which may infringe our intellectual property rights. To counter such infringement, we may advise such companies of our intellectual property rights, including, in some cases, intellectual property rights that provide protection for our lead product candidates, and demand that they stop infringing those rights. Such demand may provide such companies the opportunity to challenge the validity of certain of our intellectual property rights, or the opportunity to seek a finding that their activities do not infringe our intellectual property rights. We may also be required to file infringement actions, which can be expensive and time-consuming. In an infringement proceeding, a defendant may assert and a court may agree with a defendant that a patent of ours is invalid or unenforceable, or may refuse to stop the other party from using the intellectual property at issue. An adverse result in any litigation could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, 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 this type of litigation.

***Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.***

Our commercial success depends upon our ability and the ability of any current and future collaborators to develop, manufacture, market and sell XPOVIO and our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products or product candidates and technology, including interference proceedings before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. No litigation asserting such infringement claims is currently pending against us, and we have not been found by a court of competent jurisdiction to have infringed a third party's intellectual property rights. If we are found to infringe or think there is a risk we may be found to infringe, a third party's intellectual property rights, we could be required or choose to obtain a license from such third party to continue developing, marketing and selling our products, product candidates and technology. However, we may not be able to obtain any required license on commercially reasonable terms, or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same intellectual property licensed to us. We could be forced, including by court order, to cease commercializing the infringing intellectual property or product or to cease using the infringing technology. In addition, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing our products or product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

***We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.***

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Although we have no knowledge of any such claims being alleged to date, if such claims were to arise, litigation may be necessary to defend against any such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

***Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.***

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and 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. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

***Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.***

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to the USPTO and various foreign patent offices at various points over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we rely on our outside counsel to pay these fees when due. Additionally, the USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply with such provisions, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If such an event were to occur, it could have a material adverse effect on our business.

***If our product candidates or any of our future product candidates obtain regulatory approval, additional competitors could enter the market with generic versions of such products, which may result in a material decline in sales of our competing products.***

Under the Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Amendments") to the FDCA, a company may file an ANDA, seeking approval of a generic version of an approved innovator product. Under the Hatch-Waxman Amendments, a company may also submit an NDA under section 505(b)(2) of the FDCA that references the FDA's prior approval of the innovator product or preclinical studies and/or clinical trials that were not conducted by, or for, the sponsor and for which the sponsor has not obtained a right of reference. A 505(b)(2) NDA product may be for a new or improved version of the original innovator product. The Hatch-Waxman Amendments also provide for certain periods of regulatory exclusivity, which preclude FDA approval (or in some circumstances, FDA filing and review) of an ANDA or 505(b)(2) NDA.

In certain circumstances, third parties may file an ANDA or NDA under Section 505(b)(2) as early as the so-called "NCE-1" date that is one year before the expiry of the five-year period of New Chemical Entity exclusivity or more generally four years after NDA approval. The third parties are allowed to rely on the safety and effectiveness data of the innovator's product, may not need to conduct clinical trials and can market a competing version of a product after the expiration or loss of patent exclusivity or the expiration or loss of regulatory exclusivity and often charge significantly lower prices. Upon the expiration or loss of patent protection or the expiration or loss of regulatory exclusivity for a product, the major portion of revenues for that product may be dramatically reduced in a very short period of time. If we are not successful in defending our patents and regulatory exclusivities, we will not derive the expected benefit from them. For example, the NCE-1 date for selinexor was July 3, 2023 after which a third party could be positioned to market an ANDA or Section 505(b)(2) product that competes with selinexor prior to the expiry of our patents if the third party successfully challenged the validity of our patents protecting the product.

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 FDA publication "Approved Drug Products with Therapeutic Equivalence Evaluations," known as the Orange Book. If there are patents listed in the Orange Book for the applicable, approved innovator product, a generic or 505(b)(2) sponsor that seeks to market its product before expiration of the patents must include in their applications what is known as a "Paragraph IV" certification, challenging the validity or enforceability, or claiming non-infringement, of the listed patent or patents. Notice of the certification must be given to the patent owner and NDA holder and if, within 45 days of receiving notice, either the patent owner or NDA holder sues for patent infringement, approval of the ANDA or 505(b)(2) NDA is stayed for up to 30 months.

Accordingly, if any of our product candidates that are regulated as drugs are approved, competitors could file ANDAs for generic versions of these products or 505(b)(2) NDAs that reference our products. If there are patents listed for such drug products 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 sponsor does or does not intend to challenge the patent. We cannot predict which, if any, patents in our current portfolio or patents we may obtain in the future will be eligible for listing in the Orange Book, how any generic competitor would address such patents, whether we would sue on any such patents or the outcome of any such suit.

***If we do not successfully extend the term of patents covering our product candidates under the Hatch-Waxman Amendments and similar foreign legislation, our business may be materially harmed.***

Depending upon the timing, duration and conditions of FDA marketing approval, if any, of our products or product candidates, one or more of our U.S. patents may be eligible for patent term extension under the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term extension of up to five years for one patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, 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. The total patent term, including the extension period, may not exceed 14 years following FDA approval. Accordingly, the length of the extension, or the ability to even obtain an extension, depends on many factors.

In the U.S., only a single patent can be extended for each qualifying FDA approval, and any patent can be extended only once and only for a single product. Laws governing analogous patent term extensions in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Because both selinexor and verdinexor are protected by a single family of patents and applications, we may not be able to secure patent term extensions for both of these product candidates in all jurisdictions where these product candidates are approved.

If we are unable to obtain a patent term extension for a product or product candidate or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product or product candidate, if any, in that

jurisdiction will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue could be materially reduced.

***If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.***

In addition to seeking patents for our products, product candidates and other discoveries, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. To the extent that we are unable to timely enter into confidentiality and invention or patent assignment agreements with our employees and consultants, our ability to protect our business through trade secrets and patents may be harmed. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside of the U.S. are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed. To the extent inventions are made by a third party under an agreement that does not grant us an assignment of their rights in inventions, we may choose or be required to obtain a license.

***Not all of our trademarks are registered. Failure to secure those registrations could adversely affect our business.***

As of May 3, 2024, we have trademark registrations in the U.S. for KARYOPHARM THERAPEUTICS, our color logo, and a combination of the two, XPOVIO, PORE for our online research portal, and KARYFORWARD and our KARYFORWARD logo for our financial aid and charitable services. We also have pending applications in the U.S. to register KARYOPHARM alone, and our logo in greyscale, for pharmaceuticals. Outside of the U.S., XPOVIO is registered or pending in 46 additional jurisdictions, and is registered in Katakana in Japan, Hangul in South Korea, and Chinese characters in Taiwan. KARYOPHARM, the greyscale logo, KARYOPHARM THERAPEUTICS with the color logo, and the KARYFORWARD logo are each registered or pending in four jurisdictions outside of the U.S. We also have registrations or applications for eight additional possible drug names in numerous foreign jurisdictions. If we do not secure registrations for our trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would, which could adversely affect our business. During trademark registration proceedings in the U.S. and foreign jurisdictions, we may receive rejections. We are given an opportunity to respond to those rejections, but we may not be able to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings.

In addition, any proprietary name we propose to use with our key product candidates in the U.S. must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed drug names, including an evaluation of potential for confusion with other drug names. If the FDA objects to any of our proposed proprietary drug names for any of our product candidates, if approved, we may be required to expend significant additional resources in an effort to identify a suitable proprietary drug name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

**Risks Related to Our Operations and Employee Matters**

***Our future success depends on our ability to retain key members of our management team and to attract, retain and motivate qualified personnel.***

We are highly dependent on the management, technical and scientific expertise of principal members of our management and scientific teams, including our President and Chief Executive Officer. Although we have entered into formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees. The loss of the services of any of our key employees could impede the achievement of our research, development, commercialization and other business objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel is critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategies. Our consultants and advisors may be

employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

***Our business and operations may be materially adversely affected in the event of information technology system failures or security breaches, and the costs and consequences of implementing data protection measures could be significant.***

Despite the implementation of security measures, our internal computer systems, and those of our CROs and other third parties on which we rely, are vulnerable to damage or other impacts from cyber-attacks, computer viruses, unauthorized access, sabotage, natural disasters, fire, terrorism, war and telecommunication and electrical failures. Such systems are also vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party vendors and/or business partners, or from cyber incidents initiated by malicious third parties. Cyber incidents are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect, respond to and recover from. Cyber incidents could include the deployment of harmful malware, ransomware, denial-of-service attacks, unauthorized access to or deletion of files, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyber incidents also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient. We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company, including personal data of our employees. In addition, outside parties may attempt to penetrate our systems or those of our vendors or fraudulently induce our employees or employees of our vendors to disclose sensitive information to gain access to our data. Like other companies, we may experience threats to our data and systems, including malicious codes and viruses, and other cyber-attacks. In addition, we face other kinds of risks related to our commercial and personal data, including lost or stolen devices or other systems (including paper records) that collect and store our personal and commercial information. Furthermore, our manufacturing vendors could also be subject to a cyber-attack that could negatively impact the manufacturing process of our products and/or product candidates, which could, in turn, harm our patients, result in a product recall, or provide uncertain medical or trial results.

We are aware of certain vendors who have been impacted by cyber-attacks, inclusive of but not limited to ransomware, phishing, and spam. While such events have not directly impacted us, similar events in the future could have a material impact on us. If a cyber-attack or other security incident were to occur and cause interruptions in our operations, it could result in a material disruption of our development and commercialization programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from completed, 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 were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our reputation or competitive position could be damaged, and the further development and commercialization of our products or product candidates could be delayed or halted. We may not have adequate insurance coverage to provide compensation for any losses associated with such events. In addition, we may in certain instances be required to provide notification to individuals or others in connection with the loss of their personal or commercial information.

If a material breach of our security or that of our vendors occurs, our financial or other confidential information could be compromised, the market perception of the effectiveness of our security measures could be harmed, we could lose business, our reputation and credibility could be damaged and we could be subject to legal proceedings. In addition, the cost and operational consequences of implementing further data protection measures could be significant. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. The development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become more sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely.

**Risks Related to Our Common Stock**

***Our stock price has in the past and may in the future fail to meet minimum requirements for continued listing on the Nasdaq Global Select Market. Our ability to publicly or privately sell equity securities and the liquidity of our common stock could be adversely affected if we are delisted from the Nasdaq Global Select Market or if we are unable to transfer our listing to another stock market.***

We must satisfy Nasdaq's continued listing requirements, including, among other things, a minimum closing bid price of $1.00 per share, or risk delisting, which would have a material adverse effect on our business. There can be no assurances that we will continue to maintain compliance with the requirements for listing our common stock on Nasdaq. Any potential delisting of our common stock from the Nasdaq Global Select Market would likely result in decreased liquidity and increased volatility for our common stock and would adversely affect our ability to raise additional capital or to enter into strategic transactions. Any potential

delisting of our common stock from the Nasdaq Global Select Market would make it more difficult for our stockholders to sell our common stock in the public market.

In the past, we have received written notification from the Nasdaq Stock Market ("Nasdaq") informing us that we were not in compliance with certain continued listing requirements of the Nasdaq Global Select Market. As previously disclosed, on December 6, 2023, we received a deficiency letter from the Listing Qualifications Department (the "Staff") notifying us that, for the prior 30 consecutive business days, the bid price of our common stock had closed below the minimum $1.00 per share requirement for continued inclusion on the Nasdaq Global Select Market pursuant to Nasdaq Listing Rule 5450(a)(1) (the "Bid Price Rule"). On February 16, 2024, we received a letter from the Staff notifying us that we regained compliance with the Bid Price Rule for continued inclusion on the Nasdaq Global Select Market.

Although the minimum bid price deficiency matters is now closed, there can be no assurance that we will be able to continue to comply with the Nasdaq continued listing requirements.

***Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.***

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

***The price of our common stock has been and may continue to be volatile and your investment in our stock could decline in value or fluctuate significantly, including as a result of analysts' activities.***

Our stock price has been, and may continue to be, volatile and your investment in our stock could decline or fluctuate significantly. Our common stock price has ranged from $0.62 to $3.78 in the 52-week period ended May 3, 2024. On May 3, 2024, the closing sale price of our common stock on the Nasdaq Global Select Market was $1.13 per share. The stock market in general and the market for pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies, such as the response to world-wide economic disruptions related to the COVID-19 pandemic, the conflict between Russia and Ukraine, the war between Israel and Hamas, inflation and sustained high interest rates. The market price for our common stock may be influenced by many factors, including:

- our failure to successfully execute on our commercialization strategy for XPOVIO or our product candidates, if approved;
- the level of success of competitive products or technologies;
- results, delays in, or the halting of our clinical trials or those of our competitors, including reports of AEs related to the use of our products;
- announcements by us or our competitors of new products or data, significant mergers, acquisitions, licenses or joint ventures;
- commencement or termination of collaborations for our development programs and the commercialization of our products;
- adverse regulatory or legal developments in the U.S. and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- additions or departures of key personnel;
- the level of expenses related to the commercialization of XPOVIO and clinical development programs for any of our product candidates;
- the results of our efforts to discover, develop, acquire or in-license additional products or product candidates;
- actual or anticipated changes in estimates of financial results or guidance, clinical development timelines or recommendations by securities analysts;
- actual or anticipated fluctuations in our quarterly or annual financial results;
- changes in healthcare laws affecting pricing, reimbursement or access;
- market conditions in the pharmaceutical and biotechnology sectors, including as the result of uncertainties due to or impacts from pandemics or other public health emergencies;
- general economic, industry and market conditions, such as those caused by the ongoing conflict between Russia and Ukraine, the war between Israel and Hamas, inflation and fluctuations in interest rates;
- our ability to raise additional capital and/or refinance our debt and the terms on which we can raise capital and/or refinance debt;
- sales of large blocks of our common stock, including by our executive officers, directors and significant stockholders, or substantial changes in short interest in our common stock; and
- the other risks and uncertainties described in this "*Risk Factors*" section.

The COVID-19 pandemic caused significant disruptions in the financial markets and also impacted the volatility of our stock price and trading in our stock. In addition, U.S. and global markets are experiencing volatility and disruption following the escalation of geopolitical tensions and the ongoing conflict between Russia and Ukraine, the war between Israel and Hamas, inflation and sustained high interest rates. A continuation or worsening of the levels of market disruption and volatility could have an adverse effect on the market price of our common stock. Furthermore, the trading market for our common stock relies, in part, on the research and reports that industry or financial analysts publish about us or our business. Our stock price could decline significantly if we fail to meet or exceed analysts' forecasts and expectations or if one or more of the analysts covering our business downgrade their evaluations of our stock. Further, if one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

***Securities or other litigation could result in substantial costs and may divert management's time and attention from our business.***

Securities class action litigation is often brought against a company following a decline or periods of volatility in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years, including as a result of the COVID-19 pandemic, and we are therefore a target of this type of litigation. For example, we were subject to a class action lawsuit and a shareholder derivative lawsuit alleging federal securities laws violations, both of which have been dismissed. We may face additional securities class action litigation or other litigation in the future, including if we fail to successfully commercialize XPOVIO, or if we cannot obtain regulatory approvals for, or if we otherwise fail to successfully commercialize and launch, our product candidates.

The outcome of litigation is necessarily uncertain, and we could be forced to expend significant resources in the defense of such suits, and we may not prevail. Monitoring and defending against legal actions is time-consuming for our management and detracts from our ability to fully focus our internal resources on our business activities. In addition, we may incur substantial legal fees and costs in connection with any such litigation. We have not established any reserves for any potential liability relating to any such potential lawsuits. It is possible that we could, in the future, incur judgments or enter into settlements of claims for monetary damages. We currently maintain insurance coverage for some of these potential liabilities. Other potential liabilities may not be covered by insurance, insurers may dispute coverage or the amount of insurance may not be enough to cover damages awarded. In addition, certain types of damages may not be covered by insurance, and insurance coverage for all or certain forms of liability may become unavailable or prohibitively expensive in the future. A decision adverse to our interests on one or more legal matters or litigation could result in the payment of substantial damages, or possibly fines, and could have a material adverse effect on our reputation, financial condition and results of operations.

***We have broad discretion in the use of our cash, cash equivalents and investments and may not use them effectively.***

Our management has broad discretion to use our cash, cash equivalents and investments to fund our operations and could spend these funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use to fund our operations, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value.

***If we identify a material weakness in our internal control over financial reporting, it could have an adverse effect on our business and financial results and our ability to meet our reporting obligations could be negatively affected, each of which could negatively affect the trading price of our common stock.***

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. Accordingly, a material weakness increases the risk that the financial information we report contains material errors.

We regularly review and update our internal controls, disclosure controls and procedures, and corporate governance policies. In addition, we are required under the Sarbanes-Oxley Act of 2002 to report annually on our internal control over financial reporting. Any system of internal controls, however well designed and operated, is based in part on certain assumptions and can provide only reasonable, not absolute, assurances that the objectives of the system are met. If we, or our independent registered public accounting firm, determine that our internal control over our financial reporting is not effective, or we discover areas that need improvement in the future, or we experience high turnover of our personnel in our financial reporting functions, these shortcomings could have an adverse effect on our business and financial results, and the price of our common stock could be negatively affected.

If we cannot conclude that we have effective internal control over our financial reporting, or if our independent registered public accounting firm is unable to provide an unqualified opinion regarding the effectiveness of our internal control over financial reporting, investors could lose confidence in the reliability of our financial statements, which could lead to a decline in our stock price. Failure to comply with reporting requirements could also subject us to sanctions and/or investigations by the SEC, the Nasdaq Stock Market or other regulatory authorities.

**If the e*stimates we make, or the assumptions on which we rely, in preparing our consolidated financial statements, our projected guidance and/or our projected market opportunities prove inaccurate, our actual results may vary from those reflected in our projections and accruals.***

Our consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (“GAAP”). The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses, the amounts of charges accrued by us and related disclosure of contingent assets and liabilities. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances.

We cannot assure you, however, that our estimates, or the assumptions underlying them, will be correct. Further, from time to time we issue guidance on our expected financial performance for future periods, such as our expectations regarding our revenue, non-GAAP research and development and selling, general and administrative expenses, and cash, cash equivalents and investments available for operations, which guidance is based on estimates and the judgment of management. If, for any reason, our actual results differ materially from our guidance, we may have to adjust our publicly announced financial guidance. If we fail to meet, or if we are required to change or update any element of, our publicly disclosed financial guidance or other expectations about our business, our stock price could decline.

Further our estimates of the potential market opportunities for XPOVIO and our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment on the part of our management, are inherently uncertain and the reasonableness of these assumptions has not been assessed by an independent source. If any of our assumptions or estimates, or these publications, research, surveys or studies prove to be inaccurate, then the actual market for XPOVIO or any other products or product candidates may be smaller than we expect, and as a result our product revenue may be limited and it may be more difficult for us to achieve profitability.

***Our ability to use our net operating loss carryforwards and tax credit carryforwards to offset future taxable income may be subject to certain limitations.***

Under the provisions of the Internal Revenue Code of 1986, as amended (the "Code"), our net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service (and state tax authorities under relevant state tax rules). In addition, as described below in "Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition," the TCJA, as amended by the Coronavirus Aid, Relief and Economic Security Act (the "CARES Act"), includes changes to U.S. federal tax rates and the rules governing net operating loss carryforwards that may significantly impact our ability to utilize our net operating losses to offset taxable income in the future. Furthermore, the use of net operating loss and tax credit carryforwards may become subject to an annual limitation under Sections 382 and 383 of the Code, respectively, and similar state provisions in the event of certain cumulative changes in the ownership interest of significant stockholders in excess of 50 percent over a three-year period. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of a company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. Our company has completed several financings since its inception which resulted in an ownership change under Sections 382 and 383 of the Code. In addition, future changes in our stock ownership, some of which are outside of our control, could result in ownership changes in the future. For these reasons, we may not be able to use some or all of our net operating loss and tax credit carryforwards, even if we attain profitability.

***Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.***

Changes in tax law may adversely affect our business or financial condition. The TCJA, as amended by the CARES Act, significantly revises the Code. The TCJA, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21% and limitation of the deduction for net operating losses to 80% of current year taxable income for losses arising in taxable years beginning after December 31, 2017 and the elimination of the carryback of such losses (though any such net operating losses may be carried forward indefinitely). In addition, beginning in 2022, the TCJA eliminates the option to deduct research and development expenditures currently and requires corporations to capitalize and amortize them over five years.

In addition to the CARES Act, as part of Congress' response to the COVID-19 pandemic, economic relief legislation was enacted in 2020 and 2021 containing tax provisions. Further, as of August 2022, the IRA introduced new tax provisions, including a one percent excise tax imposed on certain stock repurchases by publicly traded companies. The one percent excise tax generally applies to any acquisition of stock by the publicly traded company (or certain of its affiliates) from a stockholder of the company in exchange for money or other property (other than stock of the company itself), subject to a de minimis exception. Thus, the excise tax could apply to certain transactions that are not traditional stock repurchases. Regulatory guidance under the TCJA and such additional legislation is and continues to be forthcoming, and such guidance could ultimately increase or lessen their impact on our business and financial condition. In addition, it is uncertain if and to what extent various states will conform to the TCJA and additional tax legislation.

**Item 5. Other Information.**

*(c) Director and Officer Trading Arrangements*

A portion of the compensation of our directors and officers (as defined in Rule 16a-1(f) under the Securities Exchange Act of 1934, as amended (the "Exchange Act")) is in the form of equity awards and, from time to time, directors and officers engage in open-market transactions with respect to the securities acquired pursuant to such equity awards or other securities of our company, including to satisfy tax withholding obligations when equity awards vest or are exercised, and for diversification or other personal reasons.

Transactions in our securities by directors and officers are required to be made in accordance with our Insider Trading Policy, which requires that the transactions be in accordance with applicable U.S. federal securities laws that prohibit trading while in possession of material nonpublic information. Rule 10b5-1 under the Exchange Act provides an affirmative defense that enables directors and officers to prearrange transactions in our securities in a manner that avoids concerns about initiating transactions while in possession of material nonpublic information.

During the first quarter of 2024, none of our directors or officers adopted or terminated a Rule 10b5-1 trading arrangement or a non-Rule 10b5-1 trading arrangement (as defined in Item 408(c) of Regulation S-K).

**Item 6. Exhibits.**

| | |
|---|---|
| 10.1* | Non-Employee Director Compensation Policy. |
| 10.2* | Offer Letter, dated as of April 4, 2022, between the Registrant and Reshma Rangwala. |
| 31.1 | Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended. |
| 31.2 | Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended. |
| 32.1 | Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. |
| 32.2 | Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. |
| 101.INS | Inline XBRL Instance Document. The instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document. |
| 101.SCH | Inline XBRL Taxonomy Extension Schema Document. |
| 101.CAL | Inline XBRL Taxonomy Extension Calculation Linkbase Document. |
| 101.DEF | Inline XBRL Taxonomy Extension Definition Linkbase Document. |
| 101.LAB | Inline XBRL Taxonomy Extension Label Linkbase Document. |
| 101.PRE | Inline XBRL Taxonomy Extension Presentation Linkbase Document. |
| 104 | Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101) |

* Indicates a management contract or compensatory plan or arrangement.

**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.

**KARYOPHARM THERAPEUTICS INC.**

Date: May 8, 2024

By: /s/ Richard Paulson
Richard Paulson
*President and Chief Executive Officer*
*(Principal executive officer)*

Date: May 8, 2024

By: /s/ Michael Mason
Michael Mason
*Executive Vice President, Chief Financial Officer and Treasurer*
*(Principal financial and accounting officer)*

**Exhibit 10.1**

**KARYOPHARM THERAPEUTICS INC.**
**NON-EMPLOYEE DIRECTOR COMPENSATION POLICY**

**Effective May 21, 2021**
**(as amended June 30, 2022, February 10, 2023 and March 14, 2024)**

The purpose of this Non-Employee Director Compensation Policy (this "***Policy***") of Karyopharm Therapeutics Inc. (the "***Company***") is to provide a total compensation package that enables the Company to attract and retain, on a long-term basis, high-caliber directors and reflect the substantial time commitment necessary to oversee the Company's affairs. In furtherance of this purpose, non-employee members of the board of directors (the "***Board***") of the Company shall be eligible to receive cash and equity compensation as set forth in this Policy. The cash compensation and equity grants described in this Policy shall be paid or be made, as applicable, automatically and without further action of the Board, to each member of the Board who is not an employee of the Company or any parent or subsidiary of the Company (each, a "***Non-Employee Director***"), unless such Non-Employee Director declines the receipt of such cash compensation or equity grants by written notice to the Company. This Policy shall be reviewed by the Compensation Committee periodically and may be amended, modified or terminated by the Board at any time in its sole discretion. The terms and conditions of this Policy shall supersede any prior cash and/or equity compensation program with respect to service as a member of the Board. This Policy shall become effective on the date set forth above, with any amendments to the Policy becoming effective on the date set forth above (such date, the "***Effective Date***").

**1. Cash Compensation**

The following annual cash retainer fees shall be paid to the Non-Employee Directors serving on the Board of Directors and the Audit Committee, Compensation Committee, Nominating, Corporate Governance & Compliance Committee, and Portfolio and Commercialization Committee, as applicable.

| | **Annual Retainer Fee (Member)** | **Annual Retainer Fee (Lead Independent Director/ Chair)** |
|---|---|---|
| **Board of Directors** | **$50,000** | **$85,000** |
| **Audit Committee** | **$10,000** | **$20,000** |
| **Compensation Committee** | **$10,000** | **$20,000** |
| **Nominating, Corporate Governance & Compliance Committee** | **$10,000** | **$20,000** |
| **Commercialization and Portfolio Committee** | **$10,000** | **$20,000** |

The annual cash compensation amount set forth above shall be earned on a quarterly basis and shall be paid in four equal quarterly installments, in arrears. If a Non-Employee Director joins the Board or a committee of the Board at a time other than effective as of the

first day of a fiscal quarter, each applicable annual retainer fee set forth above will be pro-rated based on the number of days of service in the applicable quarter.

**2. Equity Compensation**

Non-Employee Directors shall be automatically granted the equity awards described below. Each award shall be granted under and shall be subject to the terms and provisions of the Company's 2022 Equity Incentive Plan (as may be amended from time to time, the "***Plan***"), or any other successor Company equity incentive plan under which awards are permitted to be made to Non-Employee Directors. Capitalized terms used in this Section 2, but not otherwise defined, shall have the meaning ascribed to such terms in the Plan. All stock options granted to Non-Employee Directors will be non-qualified stock options, with an exercise price per share equal to 100% of the Grant Date Fair Market Value of the Common Stock on the date the option is granted, subject to such additional terms and conditions as set forth in Section 5(c) of the Plan, and have a term of ten (10) years from the date of grant (subject to earlier termination as provided in the Plan and the applicable option agreement). Each such stock option grant shall be evidenced by the Company's form of non-qualified stock option agreement used for non-employee director grants as approved by the Board.

***(a) Initial Grants***

Each new Non-Employee Director who is initially elected or appointed to the Board after the Effective Date of this Policy, shall automatically receive, on the date of such initial appointment or election to the Board (or if such date is not a market trading day, the first market trading day thereafter), a stock option to purchase a number of shares of Common Stock equal to two times the number of shares of Common Stock underlying the most recent annual stock option grant to Non-Employee Directors, as described below. Such stock option shall vest with respect to one-third of the shares on the first anniversary of the grant date and with respect to an additional 1/36th of the total number of shares underlying the grant at the end of each successive month following the first anniversary of the grant date until the third anniversary of the grant date, subject to the director's continued service to the Company (as defined in the respective stock option agreement) on the applicable vesting dates.

***(b) Annual Grants***

At the first meeting of the Board following each annual meeting of stockholders, each Non-Employee Director (whether such person is an incumbent Non-Employee Director or a newly appointed or elected Non-Employee Director) will automatically receive a stock option to purchase 69,000 shares of Common Stock (each, an "***Annual Option Grant***"); provided, however, that if a Non-Employee Director is elected or appointed to the Board at a time other than at the annual meeting of stockholders, the number of shares of Common Stock underlying the first Annual Option Grant to be received by such Non-Employee Director will be pro-rated based on the number of days served by such director on the Board from his/her start date through the date immediately preceding the next annual meeting of stockholders divided by the number of days from the last annual meeting of stockholders prior to the start date to such next annual meeting of stockholders. For example, if a new Non-Employee Director began his/her service on December 15, 2023, the

preceding annual meeting of stockholders was May 24, 2023, and the next annual meeting of stockholders is May 29, 2024, the first Annual Option Grant for such Non-Employee Director would be pro-rated to 31,295 shares (calculated as 166/366 x 69,000). Each Annual Option Grant shall vest in full on the first anniversary of the grant date, subject to the director's continued service to the Company (as defined in the respective stock option agreement) on the applicable vesting date.

***(c) Accelerated Vesting on Change in Control***

In the event that a Change in Control Event (as defined in the Plan) occurs, each stock option award that is outstanding and held by the Non-Employee Director as of the closing of such Change in Control Event shall be immediately exercisable in full.

**3.**

**Director Compensation Limits**

The aggregate amount of compensation, including both equity compensation (based on the value of such awards as calculated based on grant date fair value for financial reporting purposes) and cash compensation, granted to any Non-Employee Director in a calendar year period shall not exceed $1,000,000 for the first year of service and $750,000 for each year of Board service thereafter (or such other limit as may be set forth in the Plan, as may be amended from time to time, or any similar provision of a successor plan). Notwithstanding the foregoing, fees paid by the Company on behalf of any Non-Employee Director in connection with regulatory compliance and any amounts paid to a Non-Employee Director as reimbursement of an expense shall not count against the foregoing limit. The Board (as such term is defined in the Plan) may make exceptions to this limit for individual Non-Employee Directors in extraordinary circumstances, as the Board (as such term is defined in the Plan) may determine in its discretion, provided that the Non-Employee Director receiving such additional compensation may not participate in the decision to award such compensation. For the avoidance of doubt, this limitation shall not apply to cash or awards granted under the Plan to a Non-Employee Director in his or her capacity as an advisor or consultant to the Company.

**4. Expenses**

The Company shall reimburse each Non-Employee Director for all reasonable, documented, out-of-pocket travel and other business expenses incurred by such Non-Employee Director in connection with attending meetings of the Board, committees thereof or in connection with other Board related business.

******

**Exhibit 10.2**

85 Wells Ave. Newton, MA

April 4, 2022

Reshma Rangwala

Via Email

Dear Reshma,

I am pleased to offer you the position of **Executive Vice President and Chief Medical Officer** with Karyopharm Therapeutics Inc. (the "Company"), reporting directly to Richard Paulson. This is an important position in the Company, and I know it will be a challenging and exciting one. We anticipate your **start date to be on or around 4/18/2022**. Please review the details of your offer of employment below.

1. **Compensation**

a. *Base Salary.* Your semi-monthly **base salary will be $21,458.33 ($515,000.00, if annualized)**, subject to all applicable taxes and withholdings. This position is classified as Exempt according to the Fair Labor Standards Act (FLSA).

b. *Bonus Program.* Following the end of each calendar year, beginning in calendar year-ended 2022, and subject to the approval of the Company's Board of Directors, you may be eligible for a retention and performance **bonus of up to 40%** of your annualized base salary, based on your performance and the Company's performance during the applicable calendar year, as recommended by the Compensation Committee and approved by the Company's Board of Directors with respect to the Company's performance and as determined by your manager and approved by further department leadership with respect to your performance, in all cases in the Company's sole discretion. In any event, you must be an active employee of the Company on the date the bonus is distributed in order to be eligible for and to earn any bonus award, as it also serves as an incentive to remain employed by the Company. Any bonus would be pro-rated for the 2022 calendar year.

c. *New Hire Equity Grant.* Subject to the approval of the Compensation Committee of the Board of Directors of the Company (the "Compensation Committee"), the Company will grant you a stock option to purchase **100,000 shares** of the Company's common stock, (the "Common Stock"), at a price per share equal to the closing price per share of the Common Stock on the Nasdaq Global Select Market on the date of grant, which shall be, subject to the discretion of the Compensation Committee, on or about the last day of the month on which trading of the Common Stock occurs on the Nasdaq Global Select Market during the month in which your

employment with the Company commences (the “Grant Date”). The stock option will vest over four years at the rate of 25% on the one-year anniversary of your date of hire, with the remaining shares to vest monthly over the following three years, subject to your continued engagement with the Company on each vesting date. The stock option will be granted either (i) pursuant to the inducement grant exception set forth in NASDAQ Rule 5635(c)(4) and not pursuant to the Company’s 2013 Stock Incentive Plan or any other equity incentive plan of the Company, as an inducement that is material to your entering into employment with the Company or (ii) pursuant to the Company’s 2013 Stock Incentive Plan or a successor plan. The stock options shall be subject to such other terms and conditions of the applicable Stock Option Agreement. If granted under the Company’s 2013 Stock Incentive Plan, a successor plan, or an inducement plan, the option grant shall also be subject to the terms and conditions of such plan.

Subject to the approval of the Compensation Committee, the Company will grant you **65,000 restricted stock units (“RSUs”)** on the Grant Date. The RSUs will vest over four years at the rate of 25% on each of the four (4) consecutive anniversaries of your date of hire, subject to your continued engagement with the Company on each vesting date. The RSU will be granted either (1) pursuant to the inducement grant exception set forth in NASDAQ Rule 5635(c)(4) and not pursuant to the Company’s 2013 Stock Incentive Plan or any other equity incentive plan of the Company, as an inducement that is material to your entering into employment with the Company or (ii) pursuant to the Company’s 2013 Stock Incentive Plan or a successor plan. The RSUs shall be subject to such other terms and conditions of the applicable Restricted Stock Unit Agreement. If granted under the Company’s 2013 Stock Incentive Plan, a successor plan, or an inducement plan, the RSU grant shall also be subject to the terms and conditions of such plan.

d. You will accrue Paid Time Off (“PTO”), which includes all vacation, sick, and personal time (combined) at a rate of 13.34 hours per month, accrued on the last day of the month. This is equal to about 160 hours or 4 weeks of PTO per year. You will also receive paid holidays according to the Company’s holiday schedule.

e. *Benefits*. Commencing on your first day of employment (subject to eligibility criteria and waiting periods associated with each individual plan), you may participate in all company benefits as outlined in the Benefits at a Glance Overview which accompanies this offer letter, subject to the terms and conditions of any applicable plan documents for such benefits. The benefit programs made available by the Company, and the rules, terms and conditions for participation in such benefit plans, may be changed by the Company at any time without advance notice.

f. *2 part Sign-On Bonus*. Contingent upon the commencement of your employment and subject to the terms and conditions set forth herein, the Company agrees to pay you a one-time cash **bonus in the amount of $150,000.00**, (the "Sign on Bonus"), less all applicable taxes and withholdings, $75,000.00 of which will be paid no later than the second pay period following the commencement of your employment. The remaining $75,000.00 of the sign on bonus will be paid on or about July 15, 2022, in accordance with the Company's normal payroll practices, Provided you satisfy each of the following eligibility criteria, determined by the company's sole discretion:

1. You continue to provide satisfactory performance of all assigned duties in a competent manner and comply with Company policies and procedures.
2. You remain in compliance with this Agreement and with your Non-Disclosure, Inventions Assignment, Non-Competition, and Non-Solicitation Agreement which is effective your first day of employment (a copy of which we can provide at your request).
3. You remain continuously employed in good standing with the Company through July 15, 2021.

If for any reason you voluntarily terminate your employment with the Company or are terminated by the Company for Cause (as defined below) prior to the one-year anniversary of your start date, you will be obligated to repay the entire net amount of the Sign-On Bonus received by you.

h. *Severance Benefits*. If your employment is terminated without Cause, or you resign for Good Reason, the Company will, provided that you timely execute a severance and release of claims agreement in a form to be provided by the Company (which will include, at a minimum, a release of all releasable claims and non-disparagement, confidentiality, and cooperation obligations) (the “release agreement”) provide you with the following severance package: (a) pay you, as severance pay, the equivalent of one (1) month of your base salary as of the date of your termination from employment for every one (1) months of employment with the Company not to exceed a total of twelve (12) months of base salary regardless of the duration of your employment with the Company (the “Severance Period”); and (b) provided you elect to continue your and your eligible dependents' participation in the Company's medical and dental benefit plans pursuant to the Consolidated Omnibus Budget Reconciliation Act of 1986 ("COBRA"), the Company will pay the monthly premium to continue such coverage for the lesser of (i) the Severance Period and (ii) the end of the calendar month in which you become eligible to receive group health plan coverage under another employee benefit plan.

Notwithstanding the foregoing, if the Company (which, for the purposes of this paragraph, includes any successor entity) terminates your employment without Cause, or you resign for Good Reason within one year following the consummation of a Change in Control, then the Company (or its successor entity) will (a) pay you, as severance pay, the equivalent of twelve
(12) months of your base salary as of the date of your termination from employment (or such greater amount specified in any Company severance plan under which you are eligible), provided that you timely execute the release agreement. In each case, the release agreement must be executed and any revocation period with respect to such release agreement must expire no later than 60 days following your termination of employment. Any severance pay will be paid in the form of salary continuation in accordance with the Company’s payroll procedures, with payments beginning in the first pay period beginning after the release agreement becomes binding, provided that if the foregoing sixty (60) day period would end in a calendar year subsequent to the year in which Employee’s employment ends, payments will not begin before the first payroll period of the subsequent year; (b) pay to you an amount equal to 100% of your target annual bonus for the year in which your termination occurs, which amount shall be payable in a lump sum on the date that the first continued salary payment is made to you under your currently effective agreement with the Company; and (c) provided you elect to continue your and your eligible dependents' participation in the Company's medical and dental benefit

plans pursuant to COBRA, the Company will pay the monthly premium to continue such coverage for the lesser of (i) the Severance Period and (ii) the end of the calendar month in which you become eligible to receive group health plan coverage under another employee benefit plan.

*"Change in Control"* shall mean the sale of all or substantially all of the outstanding shares of capital stock, assets or business of the Company, by merger, consolidation, sale of assets or otherwise (other than a transaction in which all or substantially all of the individuals and entities who were beneficial owners of the capital stock of the Company immediately prior to such transaction beneficially own, directly or indirectly, more than 50% of the outstanding securities (on an as-converted to Common Stock basis) entitled to vote generally in the election of directors of the (i) resulting, surviving or acquiring corporation in such transaction in the case of a merger, consolidation or sale of outstanding shares, or (ii) acquiring corporation in the case of a sale of assets; provided that, where required for compliance with Section 409A, the event described above is also a change in control event as set forth in Treas. Reg. Section 1.409A-3(i)(5).

*"Cause"* shall mean , (i) your conviction by a court of competent jurisdiction of theft or misappropriation by you of assets of the Company, (ii) your conviction by a court of competent jurisdiction of fraud committed by you or at your direction, (iii) your conviction by a court of competent jurisdiction of, or pleading "guilty" or "no contest" to, (a) a felony or (b) any other criminal charge that has, or could be reasonably expected to have, a material adverse impact on the Company or the performance of your duties, and/or (iv) a determination by the Company in its sole discretion of (w) an act or acts of material willful misconduct by you in violation of law or government regulation in the course of your employment by the Company, ( (x) willful, repeated and material failure to perform, or gross negligence in the performance of, the duties which are reasonably assigned to you by the Company, (y) material breach of any agreement to which you and the Company are party and/or (z) failure to fully participate in a Company investigation as may be reasonably requested by the Company.

*"Good Reason"* shall mean (i) the assignment to you of any duties inconsistent in any adverse, material respect with your position, authority, duties or responsibilities as then constituted, or any other action by the Company which results in a material diminution in such position, authority, duties or responsibilities, (ii) a material reduction in your base compensation except to the extent that any such benefit is replaced with a comparable benefit, or a reduction in scope or value thereof, other than as a result of across-the board reductions or terminations affecting employees of the Company generally, or (iii) a requirement that you, without your prior consent, regularly report to work at a location that is thirty (30) miles or more away from your then current place of work; provided, however , that the conditions described immediately above in clauses (i) through (iii) shall not give rise to a termination for Good Reason, unless you have notified the Company in writing within thirty (30) days of the first occurrence of the facts and circumstances claimed to provide a basis for the termination for Good Reason, the Company has failed to correct the condition within thirty (30) days after the Company's receipt of such written notice, and you actually terminate employment with the Company within sixty (60) days of the first occurrence of the condition. For the avoidance of doubt, your required travel on the Company's business shall not be deemed a relocation of your principal office under clause (iii), above.

*Section 409A*. It is intended that this letter agreement comply with or be exempt from Section 409A of the Internal Revenue Code of 1986, and the Treasury Regulations and IRS guidance thereunder (collectively referred to as "Section 409A"), and notwithstanding anything to the contrary herein, it shall be administered, interpreted, and construed in a manner consistent with Section 409A. To the extent that any reimbursement, fringe benefit, or other, similar plan or arrangement in which you participate provides for a "deferral of compensation" within the meaning of Section 409A, (a) the amount of expenses eligible for reimbursement provided to you during any calendar year shall not affect the amount of expenses eligible for reimbursement or in-kind benefits provided to you in any other calendar year, (b) the reimbursements for expenses for which you are entitled to be reimbursed shall be made on or before the last day of the calendar year following the calendar year in which the applicable expense is incurred, (c) the right to payment or reimbursement or in-kind benefits hereunder may not be liquidated or exchanged for any other benefit, and (d) the reimbursements shall be made pursuant to objectively determinable and nondiscretionary Company policies and procedures regarding such reimbursement of expenses. If and to the extent required to comply with Section 409A, no payment or benefit required to be paid under this letter agreement on account of termination of your employment shall be made unless and until you incur a "separation from service" within the meaning of Section 409A. In the case of any amounts payable to you under this letter agreement that may be treated as payable in the form of "a series of installment payments", as defined in Treasury Regulation Section 1.409A-2(b)(2)(iii), your right to receive such payments shall be treated as a right to receive a series of separate payments for purposes of such Treasury Regulation. If any paragraph of this letter agreement provides for payment within a time period, the determination of when such payment shall be made within such time period shall be solely in the discretion of the Company. If and to the extent any portion of any payment, compensation or other benefit provided to you in connection with your employment termination is determined to constitute "nonqualified deferred compensation" within the meaning of Section 409A of the Code, and you are a specified employee as defined in Section 409A(a)(2)(B)(i) of the Code, as determined by the Company in accordance with its procedures, by which determination you hereby agree that you are bound, such portion of the payment, compensation or other benefit shall not be paid before the earlier of (i) the expiration of the six month period measured from the date of your "separation from service" (as determined under Section 409A of the Code) or (ii) the tenth day following the date of your death following such separation from service (the "New Payment Date"). The aggregate of any payments that otherwise would have been paid to you during the period between the date of separation from service and the New Payment Date shall be paid to you in a lump sum in the first payroll period beginning after such New Payment Date, and any remaining payments will be paid on their original schedule.

Withholding. The Company shall withhold from any compensation or benefits payable under this letter agreement any federal, state and local income, employment or other similar taxes as may be required to be withheld pursuant to any applicable law or regulation.

If you accept the terms of this offer, your employment with the Company constitutes at- will employment, and you are free to resign at any time, and for any or no reason. Similarly, the Company is free to terminate its employment relationship with you at any time, with or without cause. Although your job duties, title, compensation and benefits, as well as the Company's personnel policies and procedures, may change from time to time, the "at-will" nature of your

employment may only be changed by a written agreement signed by you and the Company's Chief Executive Officer or General Counsel, which expressly states the intention to modify the at-will nature of your employment. Similarly, nothing in this letter shall be construed as an agreement, either express or implied, to pay you any compensation or grant you any benefit beyond the end of your employment with the Company. We request that, in the event of resignation, you provide a notice period of at least two weeks.

Your offer is contingent upon the successful completion of an employment, and criminal background check, (which will require you to complete and sign all necessary consent forms authorizing the Company or its designee to perform these background inquiries). The Company may also require that you provide names and contact information so we may conduct reference checks about your past employment.

For purposes of federal immigration law, you will be required to provide to the Company documentary evidence of your identity and eligibility for employment in the United States. Such documentation must be provided to us within three (3) business days of your date of hire, or our employment relationship with you will be terminated.

As a condition of your employment, you are also required to sign and comply with a Non- Disclosure, Inventions Assignment, Non-Competition, and Non-Solicitation Agreement effective your first day of employment. A copy of that agreement accompanies this offer letter. Please address any concerns you may have with this agreement prior to your first day of employment at the Company. You acknowledge that your receipt of the grant of equity set forth in this offer letter is contingent upon your agreement to the non-competition provisions set forth in the Non- Disclosure, Inventions Assignment, Non-Competition, and Non-Solicitation Agreement, and that such consideration is fair and reasonable in exchange for your compliance with such non- competition obligations. In return for the compensation payments set forth in this letter, you agree to devote your full business time, best efforts, skill, knowledge, attention, and energies to the advancement of the Company's business and interests and to the performance of your duties and responsibilities as an employee of the Company and not to engage in any other business activities without prior approval from the Company.

As an employee of the Company, you will be required to comply with all Company policies and procedures. Violations of the Company's policies may lead to immediate termination of your employment. Further, the Company's premises, including all workspaces, furniture, documents, and other tangible materials, and all information technology resources of the Company (including computers, data and other electronic files, and all internet and email) are subject to oversight and inspection by the Company at any time. Company employees should have no expectation of privacy with regard to any Company premises, materials, resources, or information.

To accept the Company's offer, please sign and date this letter in the space provided. By signing this letter, you are representing that you have full authority to accept this position and perform the duties of the position without conflict with any other legal or contractual obligations, and that you are not involved in any situation that might create, or appear to create, a conflict of interest with respect to your loyalty to or duties for the Company. You additionally represent and warrant that you have not taken or shared with the Company any confidential or proprietary information belonging to any former employer or other third party, and that you will at no time

during the course of your employment with the Company use or disclose any such confidential or proprietary information of another party without that party's express consent.

This letter, together with the other documents and agreements referenced herein, sets forth all of the terms of your employment with the Company, and supersedes any prior representations or agreements including, but not limited to, any representations made during your recruitment, interviews or pre-employment negotiations, whether written or oral. This letter may not be modified or amended except by a written agreement signed by the Company and you. This offer of employment will terminate if it is not accepted, signed, and returned by close of business on 4/7/2022.

We look forward to your favorable reply and to working with you at Karyopharm!

Sincerely,

/s/ Geri Reilly

Geri Reilly
Executive Director, Talent Acquisition

Agreed to and accepted:

Signature: /s/ Reshma Rangwala

Printed Name: Reshma Rangwala

Date: Apr 4, 2022

**Exhibit 31.1**

**CERTIFICATIONS**

I, Richard Paulson, certify that:

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

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

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

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

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

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

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

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

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

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

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

/s/ Richard Paulson
Richard Paulson
*President and Chief Executive Officer*
*(Principal executive officer)*

Date: May 8, 2024

**Exhibit 31.2**

**CERTIFICATIONS**

I, Michael Mason, certify that:

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

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

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

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

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

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

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

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

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

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

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

/s/ Michael Mason

Michael Mason

*Executive Vice President, Chief Financial Officer and Treasurer*

*(Principal financial and accounting officer)*

Date: May 8, 2024

**Exhibit 32.1**

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,**
**AS ADOPTED PURSUANT TO**
**SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Quarterly Report on Form 10-Q of Karyopharm Therapeutics Inc. (the "Company") for the period ended March 31, 2024, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Richard Paulson, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to his knowledge:

(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.

/s/ Richard Paulson
Richard Paulson
*President and Chief Executive Officer*
*(Principal executive officer)*

Date: May 8, 2024

**Exhibit 32.2**

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,**
**AS ADOPTED PURSUANT TO**
**SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Quarterly Report on Form 10-Q of Karyopharm Therapeutics Inc. (the "Company") for the period ended March 31, 2024, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Michael Mason, Executive Vice President, Chief Financial Officer and Treasurer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to his knowledge:

(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.

/s/ Michael Mason
Michael Mason
*Executive Vice President, Chief Financial Officer and Treasurer*
*(Principal financial and accounting officer)*

Date: May 8, 2024