

**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 September 30, 2020

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
(State or other jurisdiction of
incorporation or organization)

85 Wells Avenue, 2nd Floor
Newton, MA
(Address of principal executive offices)

26-3931704
(I.R.S. Employer
Identification Number)

02459
(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	KPTT	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	<input type="checkbox"/>	Accelerated filer	<input checked="" type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

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 October 28, 2020, there were 73,600,777 shares of Common Stock, \$0.0001 par value per share, outstanding.

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Item 1. Condensed Consolidated Financial Statements (Unaudited).

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

	September 30, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	\$ 82,301	\$ 128,858
Short-term investments	180,743	133,098
Accounts receivable	11,062	7,862
Inventory	2,011	346
Prepaid expenses and other current assets	8,242	7,289
Restricted cash	1,088	1,117
Total current assets	285,447	278,570
Property and equipment, net	2,357	3,046
Operating lease right-of-use assets	9,694	10,617
Long-term investments	39,371	2,016
Restricted cash	718	714
Total assets	\$ 337,587	\$ 294,963
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	\$ 2,422	\$ 985
Accrued expenses	46,591	40,878
Deferred revenue	297	2,341
Operating lease liabilities	1,847	1,646
Other current liabilities	1,473	500
Total current liabilities	52,630	46,350
Convertible senior notes	115,802	109,857
Deferred royalty obligation	73,588	73,588
Operating lease liabilities, net of current portion	11,797	13,202
Deferred revenue, net of current portion	—	2,192
Total liabilities	253,817	245,189
Stockholders' equity:		
Preferred stock, \$0.0001 par value; 5,000 shares authorized; none issued and outstanding	—	—
Common stock, \$0.0001 par value; 200,000 shares authorized; 73,528 and 65,370 shares issued and outstanding at September 30, 2020 and December 31, 2019, respectively	7	7
Additional paid-in capital	1,109,350	923,142
Accumulated other comprehensive income (loss)	603	(37)
Accumulated deficit	(1,026,190)	(873,338)
Total stockholders' equity	83,770	49,774
Total liabilities and stockholders' equity	\$ 337,587	\$ 294,963

See accompanying notes to condensed consolidated financial statements.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Revenues:				
Product revenue, net	\$ 21,330	\$ 12,821	\$ 55,992	\$ 12,821
License and other revenue	3	328	16,993	9,976
Total revenues	<u>21,333</u>	<u>13,149</u>	<u>72,985</u>	<u>22,797</u>
Operating expenses:				
Cost of sales	438	1,013	1,653	1,013
Research and development	37,037	26,270	113,628	90,761
Selling, general and administrative	30,967	25,267	92,488	77,032
Total operating expenses	<u>68,442</u>	<u>52,550</u>	<u>207,769</u>	<u>168,806</u>
Loss from operations	(47,109)	(39,401)	(134,784)	(146,009)
Other income (expense):				
Interest income	600	1,137	2,424	4,320
Interest expense	(6,801)	(3,093)	(20,068)	(9,180)
Other (expense) income, net	(141)	10	(177)	(36)
Total other expense, net	<u>(6,342)</u>	<u>(1,946)</u>	<u>(17,821)</u>	<u>(4,896)</u>
Loss before income taxes	(53,451)	(41,347)	(152,605)	(150,905)
Income tax provision	(44)	(20)	(247)	(38)
Net loss	<u>\$ (53,495)</u>	<u>\$ (41,367)</u>	<u>\$ (152,852)</u>	<u>\$ (150,943)</u>
Net loss per share—basic and diluted	<u>\$ (0.73)</u>	<u>\$ (0.67)</u>	<u>\$ (2.14)</u>	<u>\$ (2.46)</u>
Weighted-average number of common shares outstanding used in net loss per share—basic and diluted	<u>73,466</u>	<u>62,093</u>	<u>71,479</u>	<u>61,297</u>

See accompanying notes to condensed consolidated financial statements.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Net loss	\$ (53,495)	\$ (41,367)	\$ (152,852)	\$ (150,943)
Comprehensive income (loss)				
Unrealized (loss) gain on investments	(319)	(59)	640	250
Foreign currency translation adjustment	31	(32)	—	(36)
Comprehensive loss	<u>\$ (53,783)</u>	<u>\$ (41,458)</u>	<u>\$ (152,212)</u>	<u>\$ (150,729)</u>

See accompanying notes to condensed consolidated financial statements.

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

	Nine Months Ended September 30,	
	2020	2019
Operating activities		
Net loss	\$ (152,852)	\$ (150,943)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	715	730
Net amortization of premiums and discounts on investments	710	(1,242)
Amortization of debt discount and issuance costs	5,945	5,298
Stock-based compensation expense	18,093	11,742
Changes in operating assets and liabilities:		
Accounts receivable	(3,200)	(7,928)
Inventory	(1,665)	(100)
Prepaid expenses and other current assets	(953)	1,108
Operating lease right-of-use assets	924	807
Accounts payable	1,437	(1,215)
Accrued expenses and other liabilities	6,686	569
Deferred revenue	(4,236)	(9,362)
Operating lease liabilities	(1,204)	(797)
Net cash used in operating activities	(129,600)	(151,333)
Investing activities		
Purchases of property and equipment	(26)	(156)
Proceeds from maturities of investments	162,855	202,454
Purchases of investments	(247,911)	(90,329)
Net cash (used in) provided by investing activities	(85,082)	111,969
Financing activities		
Proceeds from issuance of common stock, net of issuance costs	161,802	14,563
Proceeds from the exercise of stock options and shares issued under employee stock purchase plan	6,313	1,124
Proceeds from deferred royalty obligation, net	—	73,682
Net cash provided by financing activities	168,115	89,369
Effect of exchange rate on cash, cash equivalents and restricted cash	(15)	(26)
Net (decrease) increase in cash, cash equivalents and restricted cash	(46,582)	49,979
Cash, cash equivalents and restricted cash at beginning of period	130,689	118,737
Cash, cash equivalents and restricted cash at end of period	\$ 84,107	\$ 168,716
Reconciliation of cash, cash equivalents and restricted cash reported within the condensed consolidated balance sheets		
Cash and cash equivalents	\$ 82,301	\$ 168,004
Short-term restricted cash	1,088	—
Long-term restricted cash	718	712
Total cash, cash equivalents and restricted cash	\$ 84,107	\$ 168,716
Supplemental disclosures:		
Operating lease right-of-use assets obtained in exchange for operating lease liabilities	\$ —	\$ 11,711
Cash paid for amounts included in the measurement of operating lease liabilities	\$ 2,388	\$ 2,096
Cash paid for interest on deferred royalty obligation	\$ 4,521	\$ —

See accompanying notes to condensed consolidated financial statements.

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

	<u>Common Shares</u>		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at June 30, 2020	73,366	\$ 7	\$ 1,101,596	\$ 891	\$ (972,695)	\$ 129,799
Vesting of restricted stock	10	—	—	—	—	—
Exercise of stock options and shares issued under the employee stock purchase plan	152	—	1,241	—	—	1,241
Stock-based compensation expense	—	—	6,513	—	—	6,513
Unrealized loss on investments	—	—	—	(319)	—	(319)
Foreign currency translation adjustment	—	—	—	31	—	31
Net loss	—	—	—	—	(53,495)	(53,495)
Balance at September 30, 2020	<u>73,528</u>	<u>\$ 7</u>	<u>\$ 1,109,350</u>	<u>\$ 603</u>	<u>\$ (1,026,190)</u>	<u>\$ 83,770</u>
Balance at June 30, 2019	60,965	\$ 6	\$ 865,726	\$ 61	\$ (783,324)	\$ 82,469
Vesting of restricted stock	5	—	—	—	—	—
Exercise of stock options and shares issued under the employee stock purchase plan	101	—	577	—	—	577
Issuance of common stock, net of issuance costs	1,634	—	14,563	—	—	14,563
Stock-based compensation expense	—	—	3,719	—	—	3,719
Unrealized loss on investments	—	—	—	(59)	—	(59)
Foreign currency translation adjustment	—	—	—	(32)	—	(32)
Net loss	—	—	—	—	(41,367)	(41,367)
Balance at September 30, 2019	<u>62,705</u>	<u>\$ 6</u>	<u>\$ 884,585</u>	<u>\$ (30)</u>	<u>\$ (824,691)</u>	<u>\$ 59,870</u>
Balance at December 31, 2019	65,370	\$ 7	\$ 923,142	\$ (37)	\$ (873,338)	\$ 49,774
Vesting of restricted stock	199	—	—	—	—	—
Exercise of stock options and shares issued under the employee stock purchase plan	771	—	6,313	—	—	6,313
Stock-based compensation expense	—	—	18,093	—	—	18,093
Issuance of common stock, net of issuance costs	7,188	—	161,802	—	—	161,802
Unrealized gain on investments	—	—	—	640	—	640
Net loss	—	—	—	—	(152,852)	(152,852)
Balance at September 30, 2020	<u>73,528</u>	<u>\$ 7</u>	<u>\$ 1,109,350</u>	<u>\$ 603</u>	<u>\$ (1,026,190)</u>	<u>\$ 83,770</u>
Balance at December 31, 2018	60,829	\$ 6	\$ 857,156	\$ (244)	\$ (673,748)	\$ 183,170
Vesting of restricted stock	10	—	—	—	—	—
Exercise of stock options and shares issued under the employee stock purchase plan	232	—	1,124	—	—	1,124
Issuance of common stock, net of issuance costs	1,634	—	14,563	—	—	14,563
Stock-based compensation expense	—	—	11,742	—	—	11,742
Unrealized gain on investments	—	—	—	250	—	250
Foreign currency translation adjustment	—	—	—	(36)	—	(36)
Net loss	—	—	—	—	(150,943)	(150,943)
Balance at September 30, 2019	<u>62,705</u>	<u>\$ 6</u>	<u>\$ 884,585</u>	<u>\$ (30)</u>	<u>\$ (824,691)</u>	<u>\$ 59,870</u>

See accompanying 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 novel, first-in-class drugs directed against nuclear export and related targets for the treatment of cancer and other major diseases. We were incorporated in Delaware on December 22, 2008 and have a principal place of business in Newton, Massachusetts. Our **Selective Inhibitor of Nuclear Export (SINE)** compounds function by binding with and inhibiting the nuclear export protein exportin 1 (“XPO1”). Our initial focus has been on seeking the regulatory approval and commercialization of our lead SINE compound, selinexor, as an oral agent in cancer indications with significant unmet clinical need. In July 2019, the U.S. Food and Drug Administration (“FDA”) approved XPOVIO®(selinexor) tablets 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. XPOVIO became commercially available in the U.S. in July 2019. In June 2020, the FDA approved XPOVIO for a second indication to treat 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. We began commercialization of XPOVIO for this indication in June 2020. In addition, in July 2020, the FDA accepted our supplemental new drug application for XPOVIO based on the BOSTON study, which evaluated selinexor in combination with Velcade® (bortezomib) and low-dose dexamethasone in patients with multiple myeloma after at least one prior line of therapy. The FDA has assigned an action date of March 19, 2021 under the Prescription Drug User Fee Act and, if approved, we expect to launch the expanded indication immediately thereafter.

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 and nine months ended September 30, 2020 are not necessarily indicative of the results that may be expected for any other interim period or for the fiscal year ending December 31, 2020. 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, 2019 as filed with the Securities and Exchange Commission (“SEC”) on February 26, 2020 (“Annual Report”).

Basis of Consolidation

The condensed consolidated financial statements at September 30, 2020 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 on Form 10-Q are consistent with those discussed in Note 2, “*Summary of Significant Accounting Policies*,” in our Annual Report.

2. Recent Accounting Pronouncements and CARES Act Provisions

Recently Adopted Accounting Standards

In June 2016, the Financial Accounting Standards Board (“FASB”) issued Accounting Standards Update (“ASU”) No. 2016-13, *Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* (“ASU 2016-13”). Certain amendments thereto were also issued by the FASB. ASU 2016-13 and the related amendments require that credit losses be reported as an allowance using an expected loss model, representing the entity’s current estimate of credit losses expected to be incurred. The previous accounting guidance, as applied by us through December 31, 2019, was based on an incurred loss model. For available-for-sale debt securities with unrealized losses, ASU 2016-13 and the related amendments now require allowances to be recorded instead of reducing the amortized cost of the investment. ASU 2016-13 and the related amendments are effective for interim and annual fiscal periods beginning after December 15, 2019. We adopted this guidance effective January 1, 2020. The adoption of this standard did not have a material impact on our condensed consolidated financial statements.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement - Disclosure Framework-Changes to the Disclosure Requirement for Fair Value Measurement* (“ASU 2018-13”). The amendments in ASU 2018-13 modify the disclosure requirements on fair value measurements in Accounting Standards Codification (“ASC”) 820, *Fair Value Measurement*, based on the concepts in the FASB Concepts Statement, including the consideration of costs and benefits. The amendments under ASU 2018-13 are effective for interim and annual fiscal periods beginning after December 15, 2019, with early adoption permitted. We adopted this guidance effective January 1, 2020. The adoption of this standard did not have a material impact on our condensed consolidated financial statements.

Recently Issued Accounting Standard

In August 2020, the FASB issued ASU No. 2020-06, *Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity’s Own Equity (Subtopic 815-40)* (“ASU 2020-06”). ASU 2020-06 reduces complexity of accounting for convertible debt and other equity-linked instruments. For certain convertible debt instruments with a cash conversion feature, the changes are a trade-off between simplifications in the accounting model, including no separation of an “equity” component to impute a market interest rate, as well as simpler analysis of embedded equity features, and a potentially adverse impact to diluted earnings per share (“EPS”) by requiring the use of the if-converted method. The new standard will also impact other financial instruments commonly issued by both public and private companies. For example, the separation model for beneficial conversion features is eliminated, simplifying the analysis for issuers of convertible debt and convertible preferred stock. Also, certain specific requirements to achieve equity classification and/or qualify for the derivative scope exception for contracts indexed to an entity’s own equity are removed, enabling more freestanding instruments and embedded features to avoid mark-to-market accounting. As a result, the new standard may affect net income and EPS and, therefore performance measures, whether GAAP or non-GAAP, and increase debt levels, which may impact debt covenant compliance. The new standard is effective for companies that are SEC filers (excluding smaller reporting companies) for fiscal years beginning after December 15, 2021 and interim periods within that year, and two years later for other companies. Companies can early adopt the standard at the start of a fiscal year beginning after December 15, 2020. The standard can either be adopted on a modified retrospective or a full retrospective basis. We are currently evaluating the effects the adoption of ASU 2020-06 will have on our condensed consolidated financial statements and related disclosures.

CARES Act

In March 2020, the Coronavirus Aid, Relief, and Economic Security (“CARES”) Act was signed into law and provides an estimated \$2.2 trillion to fight the COVID-19 pandemic and stimulate the U.S. economy. The business tax provisions of the CARES Act include temporary changes to income and non-income-based tax laws. Some of the key income tax provisions include (1) eliminating 80% of taxable income limitations by allowing corporate entities to fully utilize net operating loss (“NOL”) carryforwards to offset taxable income in 2020, 2019 or 2018 and reinstating it for tax years after 2020; (2) allowing NOLs generated in 2020, 2019 or 2018 to be carried back five years; (3) increasing the net interest expense deduction limit to 50% of adjusted taxable income from 30% for the 2020 and 2019 tax years; (4) allowing taxpayers with alternative minimum tax credits to claim a refund for the entire amount of the credit instead of recovering the credit through refunds over a period of years, as required by the 2017 Tax Cut and Jobs Act; and (5) allowing entities to deduct more of their charitable cash contributions made during calendar year 2020 by increasing the taxable income limitation to 25% from 10%. Companies are required to account for these provisions in the period that includes the March 2020 enactment date (i.e., the first quarter for calendar year-end entities). We have assessed the impact of these provisions and they are not material to our condensed consolidated financial statements or related disclosures.

Measures not related to income-based taxes within the CARES Act include (1) allowing an employer to pay its share of Social Security payroll taxes that would otherwise be due from the date of enactment through December 31, 2020 over the following two years and (2) allowing eligible employers subject to closure due to the COVID-19 pandemic to receive a 50% credit on qualified wages against their employment taxes each quarter, with any excess credits eligible for refunds. These measures of the CARES Act also are not material to our condensed consolidated financial statements or related disclosures.

3. Product Revenue

To date, our only source of product revenue has been from the U.S. sales of XPOVIO, which we began shipping to our customers in July 2019. 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):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Gross product revenue	\$ 25,322	\$ 14,960	\$ 66,440	\$ 14,960
Provision for product revenue	(3,992)	(2,139)	(10,448)	(2,139)
Total product revenue, net	\$ 21,330	\$ 12,821	\$ 55,992	\$ 12,821

As of September 30, 2020 and December 31, 2019, net product revenue of \$11.1 million and \$7.9 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 our accounts receivables as of September 30, 2020 and December 31, 2019.

4. Inventory

The following table presents our inventory of XPOVIO (in thousands):

	September 30, 2020	December 31, 2019
Raw materials and work in process	\$ 1,566	\$ 273
Finished goods	445	73
Total inventory	\$ 2,011	\$ 346

As of September 30, 2020 and December 31, 2019, all of our inventory was related to XPOVIO, which was initially approved by the FDA in July 2019 and at which time we began to capitalize costs to manufacture XPOVIO. Prior to FDA approval of XPOVIO, all costs related to the manufacturing of XPOVIO and related material were charged to research and development expense in the period incurred. As of September 30, 2020 and December 31, 2019, we determined that a reserve related to XPOVIO inventory was not required.

5. License and Asset Purchase Agreements

In prior periods, we entered into out-licensing and asset purchase agreements with Anivive Lifesciences, Inc. (“Anivive”), Ono Pharmaceutical Co., Ltd. (“Ono”), Biogen MA Inc. (“Biogen”), and Antengene Therapeutics Limited (“Antengene”), all of which are accounted for within the scope of ASC 606, *Revenue from Contracts with Customers* (“ASC 606”). For further details on the terms and accounting treatment considerations for these contracts, please refer to Note 11, “*License and Asset Purchase Agreements*,” to our Consolidated Financial Statements contained in Item 8 of our Annual Report.

In April 2020, we terminated our October 2017 license agreement with Ono for the development and commercialization of selinexor and eltanexor for all human oncology indications in Japan, South Korea, Taiwan, Hong Kong, and the countries in the Association of Southeast Asian Nations. Subsequent to termination, all rights to selinexor and eltanexor were returned to us and no further consideration was exchanged between the parties. Accordingly, we recognized \$2.2 million in license and other revenue during the nine months ended September 30, 2020, which represented the deferred revenue on the contract as of the date of termination.

In May 2020, we entered into an amendment to our May 2018 license agreement with Antengene (the “Original Antengene Agreement” and, as amended, the “Amended Antengene Agreement”) to expand the territory for the exclusive development and commercialization rights of selinexor, eltanexor and KPT-9274, each for the diagnosis, treatment and/or prevention of all human oncology indications, as well as verdinexor for the diagnosis, treatment and/or prevention of certain human non-oncology indications (“Antengene Licensed Compounds”). Under the terms of the Original Antengene Agreement, we received an upfront cash payment of \$11.7 million.

Under the terms of the Amended Antengene Agreement, Antengene now has the exclusive development and commercialization rights for selinexor, eltanexor, KPT-9274 and verdinexor in mainland China, Taiwan, Hong Kong, Macau, South Korea, Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, Philippines, Singapore, Thailand, Vietnam, Australia and New Zealand (the “Antengene Territory”). Previously, Antengene’s territory covered mainland China and Macau for selinexor and eltanexor and mainland China, Taiwan, Hong Kong, Macau, South Korea, Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, Philippines,

Singapore, Thailand, and Vietnam for KPT-9274 and verdinexor. Furthermore, we received a one-time upfront cash payment of \$11.7 million in June 2020 and are entitled to future milestone payments from Antengene if certain development, regulatory and commercialization goals are achieved. Finally, we are also eligible to receive tiered double-digit royalties based on future net sales of selinexor and eltanexor, and tiered single- to double-digit royalties based on future net sales of verdinexor and KPT-9274 in the Antengene Territory.

We assessed the Amended Antengene Agreement in accordance with ASC 606 and concluded that the amendment was a contract modification. We further concluded that the performance obligations under the Amended Antengene Agreement were the same performance obligations identified in the Original Antengene Agreement, as disclosed in Note 11, "License and Asset Purchase Agreements," to our Consolidated Financial Statements contained in Item 8 of our Annual Report. Under the Original Antengene Agreement, we had already fulfilled all of our promises under the combined performance obligations for selinexor and KPT-9274. Accordingly, the licenses to the incremental territories for selinexor and KPT-9274 were considered distinct from the promised goods and services already provided. By contrast, we have not yet fulfilled all of our promises under the combined performance obligations for eltanexor and verdinexor under the Original Antengene Agreement. Accordingly, the licenses to the incremental territories for eltanexor and verdinexor are not distinct from promised goods and services already provided.

Based on the conclusions noted, we updated the transaction price, which includes the \$1.3 million unrecognized deferred revenue from the \$11.7 million upfront payment we received from Antengene under the terms of the Original Antengene Agreement, and the \$11.7 million upfront payment we received from Antengene under the terms of the Amended Antengene Agreement, and allocated the total, or \$13.0 million, to the remaining performance obligations based on their estimated standalone selling prices as of the effective date of the Amended Antengene Agreement. Since we had already fulfilled all of our promises under the combined performance obligations for selinexor and KPT-9274 as of the effective date of the Amended Antengene Agreement, we recognized a cumulative adjustment to license revenue of \$12.7 million during the nine months ended September 30, 2020. For the remaining promises to be fulfilled under the combined performance obligation for eltanexor, we adjusted short-term deferred revenue to \$0.3 million as of September 30, 2020. We will recognize such revenue when initial clinical supply of eltanexor is delivered to Antengene, which we expect to be within twelve months from September 30, 2020. For the remaining promises to be fulfilled under the combined performance obligation for verdinexor, none of the transaction price was allocated thereto, as it was assessed as immaterial in comparison to the other combined performance obligations under the Amended Antengene Agreement.

Finally, we also reassessed other promised goods and services within the modified contract, including customer options and material rights, ultimately concluding such promised goods and services continue to be immaterial. The future regulatory and commercial milestones, both of which represent variable consideration, were evaluated under the most likely amount method, and were not included in the transaction price at contract inception and/or through September 30, 2020, because the amounts were fully constrained as of September 30, 2020. As part of our evaluation of the constraint, we considered numerous factors, including that receipt of such amounts is outside of our control. Separately, any consideration related to sales-based milestones, as well as royalties on net sales upon commercialization of XPOVIO by Antengene, will be recognized when the related sales occur, as they were determined to relate predominantly to the intellectual property licenses granted to Antengene and, therefore, have also been excluded from the transaction price in accordance with the sales-based royalty exception, as well as our accounting policy. We will re-evaluate the transaction price in each reporting period, as uncertain events are resolved, or as other changes in circumstances occur.

In summary, we recognized \$14.9 million in license and other revenue for the nine months ended September 30, 2020, related to the license agreements with Ono and Antengene described above.

As summarized in the following table, which presents changes in balance sheet accounts for our out-licensing and asset purchase agreements, we recognized \$2.3 million under the Original Antengene Agreement and \$2.2 million upon termination of the license agreement with Ono during the nine months ended September 30, 2020 (in thousands):

	December 31, 2019	Additions	Deductions	September 30, 2020
Short-term Deferred Revenue				
Original Antengene Agreement	\$ 2,341	\$ —	\$ (2,341)	\$ —
Amended Antengene Agreement	—	297	—	297
Total short-term deferred revenue	<u>\$ 2,341</u>	<u>\$ 297</u>	<u>\$ (2,341)</u>	<u>\$ 297</u>
Long-term Deferred Revenue				
Ono	\$ 2,192	\$ —	\$ (2,192)	\$ —
Total long-term deferred revenue	<u>\$ 2,192</u>	<u>\$ —</u>	<u>\$ (2,192)</u>	<u>\$ —</u>
Total deferred revenue	<u>\$ 4,533</u>	<u>\$ 297</u>	<u>\$ (4,533)</u>	<u>\$ 297</u>

6. Fair Value of Financial Instruments

Financial instruments, including cash, restricted cash, prepaid expenses and other current assets, accounts payable and accrued expenses, are presented at amounts that approximate fair value at September 30, 2020 and December 31, 2019.

We are required to 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 of the investments and is not a measure of the investment credit quality. The hierarchy defines three levels of valuation inputs:

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

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

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

Our cash equivalents are comprised of money market funds and U.S. government and agency securities. We measure these investments at fair value. The fair value of cash equivalents held in money market funds and U.S. treasury securities is determined based on "Level 1" inputs.

Items classified as Level 2 within the valuation hierarchy consist of commercial paper, corporate debt securities, and U.S. government and agency securities. We estimate the fair values 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 our deferred royalty obligation, as discussed further in Note 11, "*Long-Term Obligations*", is measured at fair value using an option pricing Monte Carlo simulation model and is included as a component of the deferred royalty obligation. 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 interest and other income (expense), net. The assumptions used in the option pricing Monte Carlo simulation model include: (1) our estimates of the probability and timing of related events; (2) the probability-weighted net sales of XPOVIO and any of our other future products, including worldwide net product sales and upfront payments, milestones and royalties; (3) our risk-adjusted discount rate that includes a company specific risk premium; (4) our cost of debt; (5) volatility; and (6) the probability of a change in control occurring during the term of the instrument. Our embedded derivative liability, as well as the estimated fair value of the deferred royalty obligation, is described in Note 2, "*Summary of Significant Accounting Policies*," and Note 15, "*Long-Term Obligations*" to our Consolidated Financial Statements contained in Item 8 of our Annual Report.

The following table presents information about our financial assets and liability that have been measured at fair value at September 30, 2020 and indicates the fair value hierarchy of the valuation inputs utilized to determine such fair value (in thousands):

<u>Description</u>	<u>Total</u>	<u>Quoted Prices in Active Markets (Level 1)</u>	<u>Significant Other Observable Inputs (Level 2)</u>	<u>Significant Unobservable Inputs (Level 3)</u>
Financial assets				
Cash equivalents:				
Money market funds	\$ 29,555	\$ 29,555	\$ —	\$ —
U.S. government and agency securities	8,998	8,998	—	—
Investments:				
Short-term:				
Corporate debt securities	134,750	—	134,750	—
Commercial paper	42,974	—	42,974	—
U.S. government and agency securities	3,019	—	3,019	—
Long-term:				
Corporate debt securities (one to two-year maturity)	38,467	—	38,467	—
U.S. government and agency securities (one to two-year maturity)	904	—	904	—
	<u>\$ 258,667</u>	<u>\$ 38,553</u>	<u>\$ 220,114</u>	<u>\$ —</u>
Financial liability				
Embedded derivative liability	\$ 2,300	\$ —	\$ —	\$ 2,300

The following table presents information about our financial assets and liability that have been measured at fair value at December 31, 2019 and indicates the fair value hierarchy of the valuation inputs utilized to determine such fair value (in thousands):

<u>Description</u>	<u>Total</u>	<u>Quoted Prices in Active Markets (Level 1)</u>	<u>Significant Other Observable Inputs (Level 2)</u>	<u>Significant Unobservable Inputs (Level 3)</u>
Financial assets				
Cash equivalents:				
Money market funds	\$ 71,380	\$ 71,380	\$ —	\$ —
Investments:				
Short-term:				
Corporate debt securities	89,079	—	89,079	—
Commercial paper	39,022	—	39,022	—
U.S. government and agency securities	4,997	—	4,997	—
Long-term:				
Corporate debt securities (one to two-year maturity)	2,016	—	2,016	—
	<u>\$ 206,494</u>	<u>\$ 71,380</u>	<u>\$ 135,114</u>	<u>\$ —</u>
Financial liability				
Embedded derivative liability	\$ 2,300	\$ —	\$ —	\$ 2,300

7. Investments

The following table summarizes our investments in corporate debt securities, commercial paper, and U.S. government and agency securities, classified as available-for-sale, as of September 30, 2020 (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Loss	Fair Value
Short-term:				
Corporate debt securities	\$ 134,394	\$ 371	\$ (15)	\$ 134,750
Commercial paper	42,969	6	(1)	42,974
U.S. government and agency securities	3,014	5	—	3,019
Long-term:				
Corporate debt securities (one to two-year maturity)	38,207	277	(17)	38,467
U.S. government and agency securities (one to two-year maturity)	898	6	—	904
	<u>\$ 219,482</u>	<u>\$ 665</u>	<u>\$ (33)</u>	<u>\$ 220,114</u>

The following table summarizes our investments in corporate debt securities, commercial paper, and U.S. government and agency securities, classified as available-for-sale as of December 31, 2019 (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Loss	Fair Value
Short-term:				
Corporate debt securities	\$ 89,110	\$ 12	\$ (43)	\$ 89,079
Commercial paper	39,004	18	—	39,022
U.S. government and agency securities	4,990	7	—	4,997
Long-term:				
Corporate debt securities (one to two-year maturity)	2,017	—	(1)	2,016
	<u>\$ 135,121</u>	<u>\$ 37</u>	<u>\$ (44)</u>	<u>\$ 135,114</u>

We review investments whenever the fair value of an investment is less than the amortized cost and evidence indicates that an investment's carrying amount is not recoverable within a reasonable period of time. 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 security is compared to the amortized cost basis of the security. 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 for the credit loss 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 income (loss).

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 available-for-sale security is confirmed or when either of the criteria regarding intent or requirement to sell is met. The unrealized losses at September 30, 2020 and December 31, 2019 were attributable to changes in interest rates and we do not believe any unrealized losses represent credit losses.

We held 27 commercial paper and corporate debt securities at both September 30, 2020 and December 31, 2019, that were in an unrealized loss position. The following table summarizes these available-for-sale securities in an unrealized loss position for which an allowance for credit losses has not been recorded at September 30, 2020, aggregated by major security type and length of time in a continuous unrealized loss position (in thousands):

	Less than 12 Months		12 Months or Longer		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
Commercial paper	\$ 11,987	\$ (1)	\$ —	\$ —	\$ 11,987	\$ (1)
Corporate debt securities	50,709	(32)	—	—	50,709	(32)
Total	<u>\$ 62,696</u>	<u>\$ (33)</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 62,696</u>	<u>\$ (33)</u>

8. Net Loss Per Share

Basic and diluted net loss per common share is calculated by dividing net loss by the weighted-average number of common shares outstanding during the period, without consideration for common stock equivalents. Our potentially dilutive shares, which include outstanding stock options and unvested restricted stock units, are considered to be common stock equivalents and are only included in the calculation of diluted net loss per share when their effect is dilutive.

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

	As of September 30,	
	2020	2019
Outstanding stock options	11,180	10,211
Unvested restricted stock units	1,631	835

We have the option to settle the conversion obligation for our 3.00% convertible senior notes issued October 2018, and due 2025, in cash, shares or any combination of the two. As such notes were not convertible as of September 30, 2020, they are not participating securities and do not have an impact on the calculation of basic loss per share. Based on our net loss position, there was no impact to the calculation of dilutive loss per share during the three and nine months ended September 30, 2020 and 2019.

9. Stock-based Compensation

The following table summarizes stock-based compensation expenses included in operating expenses for the periods indicated (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Cost of sales	\$ 29	\$ 27	\$ 91	\$ 27
Research and development	2,687	1,593	7,668	4,785
Selling, general and administrative	3,797	2,099	10,334	6,930
Total stock-based compensation	\$ 6,513	\$ 3,719	\$ 18,093	\$ 11,742

10. Equity

Underwritten Offerings

On March 6, 2020, we completed a follow-on offering under our shelf registration statement on Form S-3 pursuant to which we issued an aggregate of 7,187,500 shares of common stock, which included the full exercise of the underwriters' option to purchase additional shares, at a public offering price of \$24.00 per share. We received aggregate net proceeds of approximately \$161.8 million from the offering after deducting the underwriting discounts and commissions and other offering expenses.

Open Market Sale Agreement

On August 17, 2018, we entered into an Open Market Sale Agreement (the "Open Market Sale Agreement") with Jefferies LLC, as agent ("Jefferies"), pursuant to which we may issue and sell shares of our common stock having an aggregate offering price of up to \$75.0 million from time to time through Jefferies (the "Open Market Offering"). On May 5, 2020, we entered into Amendment No. 1 to the Open Market Sale Agreement, pursuant to which we increased the maximum aggregate offering price of shares of our common stock that we may issue and sell from time to time through Jefferies, by \$100.0 million, from \$75.0 million to up to \$175.0 million (the "Open Market Shares").

Under the Open Market Sale Agreement, Jefferies may sell the Open Market 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 Open Market Shares in amounts and at times to be determined by us from time to time subject to the terms and conditions of the Open Market Sale Agreement, but we have no obligation to sell any of the Open Market Shares in an Open Market Offering.

We or Jefferies may suspend or terminate the offering of Open Market 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 Open Market Shares in the amount of up to 3.0% of gross proceeds from the sale of the Open Market Shares pursuant to the Open Market Sale Agreement. We have also agreed to provide Jefferies with customary indemnification and contribution rights.

We did not sell Open Market Shares under the Open Market Sale Agreement during the three and nine months ended September 30, 2020. We sold an aggregate of 1.6 million Open Market Shares under the Open Market Sale Agreement, for net proceeds of approximately \$14.6 million, during the three and nine months ended September 30, 2019.

11. Long-Term Obligations

3.00% Convertible Senior Notes due 2025

In October 2018, we issued \$172.5 million aggregate principal amount of convertible senior notes due 2025 (the "Notes"). The Notes were sold in a private offering to qualified institutional buyers in reliance on Rule 144A under the Securities Act. In accordance with accounting guidance for debt with conversion and other options, we separately account for the liability component ("Liability Component") and the embedded conversion option ("Equity Component") of the Notes by allocating the proceeds between the Liability Component and the Equity Component, due to our ability to settle the Notes in cash, shares of our common stock or a combination of cash and shares of our common stock, at our option. In connection with the issuance of the Notes, we incurred approximately \$5.6 million of debt issuance costs, which primarily consisted of underwriting, legal and other professional fees, and allocated these costs between the Liability Component and the Equity Component based on the allocation of the proceeds. Of the total debt issuance costs, \$2.2 million was allocated to the Equity Component and recorded as a reduction to additional paid-in capital, and \$3.4 million was allocated to the Liability Component and recorded as a reduction of the Notes. The portion allocated to the Liability Component is amortized to interest expense using the effective interest method over seven years.

The Notes are senior unsecured obligations and bear interest at a rate of 3.00% per year, payable semi-annually in arrears on April 15 and October 15 of each year, beginning on April 15, 2019. The Notes will be subject to redemption at our option, on or after October 15, 2022, in whole or in part, if the conditions described below are satisfied. The 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 Notes may be converted at an initial conversion rate of 63.0731 shares of common stock per \$1 principal amount of the Notes (equivalent to an initial conversion price of approximately \$15.85 per share of common stock).

Holders of the Notes may convert all or any portion of their Notes, in multiples of \$1 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 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 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 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 Notes.

As of September 30, 2020, none of the above circumstances had occurred and as such, the Notes could not have been converted.

We may not redeem the Notes prior to October 15, 2022. On or after October 15, 2022, we may redeem for cash all or part of the 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 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.

The initial carrying amount of the Liability Component of \$101.2 million was calculated by measuring the fair value of a similar liability that does not have an associated convertible feature. The allocation was performed in a manner that reflected our non-convertible borrowing rate for similar debt. The \$67.9 million Equity Component of the Notes was recognized as a debt discount and represents the difference between \$172.5 million proceeds from the issuance of the Notes and approximately \$104.7 million fair value of the liability of the Notes on their respective dates of issuance. The excess of the principal amount of the Liability Component over its carrying amount is amortized to interest expense using the effective interest method over seven years. The Equity Component is not remeasured as long as it continues to meet the conditions for equity classification.

The outstanding balances of the Notes as of September 30, 2020 consisted of the following (in thousands):

	<u>Outstanding Balances</u>
Liability component:	
Principal	\$ 172,500
Less: debt discount and issuance costs, net	(56,698)
Net carrying amount	<u>\$ 115,802</u>
Equity component:	<u>\$ 65,641</u>

We determined the expected life of the Notes was equal to its seven-year term. The effective interest rate on the Liability Component of the Notes was 11.85%. As of September 30, 2020, the “if-converted value” did not exceed the remaining principal amount of the Notes. The fair value of the 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 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 Notes as of September 30, 2020 was approximately \$206.4 million.

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

	<u>Three Months Ended September 30,</u>		<u>Nine Months Ended September 30,</u>	
	<u>2020</u>	<u>2019</u>	<u>2020</u>	<u>2019</u>
Contractual interest expense	\$ 1,293	\$ 1,300	\$ 3,881	\$ 3,882
Amortization of debt discount	1,929	1,703	5,661	5,045
Amortization of debt issuance costs	97	86	284	253
Total interest expense	<u>\$ 3,319</u>	<u>\$ 3,089</u>	<u>\$ 9,826</u>	<u>\$ 9,180</u>

Future minimum payments on the Notes as of September 30, 2020 were as follows (in thousands):

<u>Years ended December 31,</u>	<u>Future Minimum Payments</u>
2020	\$ 2,588
2021	5,175
2022	5,175
2023	5,175
2024 and thereafter	182,850
Total minimum payments	\$ 200,963
Less: interest	(28,463)
Less: unamortized discount	(56,698)
Convertible senior notes	<u>\$ 115,802</u>

Deferred Royalty Obligation

In September 2019, we entered into a Revenue Interest Financing Agreement (“deferred royalty obligation”) with HealthCare Royalty Partners III, L.P. and HealthCare Royalty Partners IV, L.P. (“HCR”) whereby HCR receives payments from us at a tiered percentage (the “Applicable Tiered Percentage”) of net revenues of XPOVIO and any of our other future products, including worldwide net product sales and upfront payments, milestones, and royalties. We received \$75.0 million upon closing (the “First Investment Amount”) and have the right to receive an additional \$75.0 million (the “Second Investment Amount”) and together with the First Investment Amount, the “Investment Amount”) upon the achievement of future regulatory and commercial milestones and subject to the approval of both parties.

In exchange for the First Investment Amount, HCR receives tiered royalties in the mid-single digits based on worldwide net revenues of XPOVIO and any of our other future products, including worldwide net product sales and upfront payments, milestones, and royalties. The Applicable Tiered Percentages are subject to reduction in the future if a target based on cumulative U.S. net sales is met. Total royalty payments are capped at 185% of the Investment Amount.

If HCR has not received 65% of the Investment Amount by December 31, 2022 or 100% of the Investment Amount by December 31, 2024, we must make a cash payment sufficient to gross up the payments to such minimum amounts.

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 and expires on the earlier of (i) the date in which HCR has received cash payments totaling an aggregate of 185% of the Investment Amount or (ii) the legal maturity date of October 1, 2031. If HCR has not received payments equal to 185% of the Investment Amount by the twelve-year anniversary of the initial closing date, we shall pay an amount equal to the Investment Amount plus a specific annual rate of return less payments previously received. As of September 30, 2020, we have made \$4.6 million in payments to HCR.

We have evaluated the terms of the deferred royalty obligation and concluded that the features of the Investment Amount are similar to those of a debt instrument. Accordingly, we have accounted for the transaction as long-term debt. We have evaluated the terms of the debt and determined that the repayment of 185% of the Investment Amount, 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. We determine the fair value of the derivative using an option pricing Monte Carlo simulation model taking into account the probability of change of control occurring and potential repayment amounts and timing of such payments that would result under various scenarios, as further described in Note 2, "*Summary of Significant Accounting Policies*" and Note 15, "*Long-Term Obligations*" to our Consolidated Financial Statements contained in Item 8 of our Annual Report. The aggregate fair value of the embedded derivative is \$2.3 million and is included in deferred royalty obligation. We remeasure the embedded derivative to fair value each reporting period until the time the features lapse and/or the termination of the deferred royalty obligation.

The effective interest rate as of September 30, 2020 was approximately 18.1%. In connection with the deferred royalty obligation, we incurred debt issuance costs totaling \$1.4 million in the quarter ended September 30, 2019. 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 assumptions used in determining the expected repayment term of the debt and amortization period of the issuance costs require that we make estimates that could impact the short and long-term classification of these costs, as well as the period over which these costs will be amortized.

The carrying value of the deferred royalty obligation, as presented on our condensed consolidated balance sheet, approximates fair value at September 30, 2020 and was measured using Level 3 inputs. The estimated fair market value was calculated using an option pricing Monte Carlo simulation model with inputs consistent with those used in determining the embedded derivative values as described in Note 2, "*Summary of Significant Accounting Policies*" and Note 15, "*Long-Term Obligations*" to our Consolidated Financial Statements contained in Item 8 of our Annual Report.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our 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, 2019, or Annual Report.

FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q, including the following discussion, contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Quarterly Report on Form 10-Q, including statements regarding possible achievement of discovery and development milestones, including regulatory submissions and approvals, our future discovery and development efforts, our commercialization efforts, our collaborations and partnering agreements with third parties, our strategy, our future operations, financial position and revenues, projected costs, prospects, plans and objectives of management, are forward looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Forward-looking statements are not guarantees of future performance and our actual results could differ materially from the plans, intentions, expectations or results discussed in the forward-looking statements. Factors that could cause actual results to differ materially from those in the forward-looking statements include, but are not limited to, our ability to successfully commercialize XPOVIO® (selinexor) tablets; the impact of the ongoing COVID-19 pandemic on our business, including decreasing sales of XPOVIO, interrupting or delaying research and development efforts, impacting the ability to procure sufficient supply for the development and commercialization of selinexor or other product candidates, delaying ongoing or planned clinical trials, impeding the execution of business plans, planned regulatory milestones and timelines, or inconveniencing patients; the adoption of XPOVIO in the commercial marketplace; adverse results in our drug discovery and clinical development activities; decisions made by the U.S. Food and Drug Administration, or FDA, and other regulatory authorities with respect to the development and commercialization of our drug candidates; our ability to raise additional capital to support our clinical development program and other operations; our ability to develop products of commercial value and to identify, discover and obtain rights to additional potential product candidates; our ability to obtain, maintain and enforce our intellectual property rights; the outcome of research and development activities and the fact that the preclinical and clinical testing of our compounds may not be predictive of the success of later clinical trials; our reliance on third-parties; competitive developments; the effect of current and future legislation and regulation and regulatory actions; as well as other risks described in this Quarterly Report on Form 10-Q, our Annual Report on Form 10-K, as filed with the Securities and Exchange Commission, or SEC, on February 26, 2020, and other filings with the SEC.

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.

OVERVIEW

We are a commercial-stage pharmaceutical company pioneering novel cancer therapies and dedicated to the discovery, development and commercialization of novel, first-in-class drugs directed against nuclear transport and related targets for the treatment of cancer and other major 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 **Selective Inhibitor of Nuclear Export (SINE)** compounds that inhibit the nuclear export protein exportin 1, or 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 high unmet medical need diseases. Our SINE compounds were the first oral XPO1 inhibitors in clinical development and to receive marketing approval in the U.S. In July 2019, our lead asset, XPOVIO, received marketing approval by the FDA in combination with dexamethasone to treat 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, or PIs, at least two immunomodulatory agents, or IMiDs, and an anti-CD38 monoclonal antibody. We refer to myeloma that is refractory to these five agents as penta-refractory myeloma. This indication was approved under the FDA's Accelerated Approval Program based on response rate and was supported by data from the STORM (**S**elinexor **T**reatment of **R**efractory **M**yeloma) study. In addition to the FDA approval of our first New Drug Application, or NDA, we also filed a Marketing Authorization Application, or MAA, with the European Medicines Agency, or EMA, in January 2019, based on the STORM data, as discussed in more detail below. Continued approval in the U.S. for this indication is contingent upon verification and description of clinical benefit in a confirmatory trial. The FDA has agreed that the randomized Phase 3 BOSTON (**B**ortezomib, **S**elinexor and **D**examethasone) study evaluating selinexor in combination with Velcade® (bortezomib) and low-dose dexamethasone in patients with multiple myeloma after at least one prior line of therapy could serve as the confirmatory trial

based on the positive top-line data announced in March 2020. In July 2020, the FDA accepted our supplemental new drug application, or sNDA, for XPOVIO, based on the BOSTON study, to treat patients with multiple myeloma after at least one prior line of therapy. The FDA has assigned an action date of March 19, 2021 under the Prescription Drug User Fee Act, or PDUFA, and, if approved, we expect to launch the expanded indication immediately thereafter.

In June 2020, XPOVIO was approved by the FDA for a second indication to treat adult patients with relapsed or refractory diffuse large B-cell lymphoma, or DLBCL, not otherwise specified, including DLBCL arising from follicular lymphoma, after at least two lines of systemic therapy. We began commercialization of this indication in June 2020. This indication was approved under the FDA's Accelerated Approval Program based on response rate and was supported by data from the SADAL (Selinexor Against Diffuse Aggressive Lymphoma) study. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. The FDA has agreed that the XPORT-DLBCL-030 study could serve as the confirmatory trial for evaluating selinexor in DLBCL. This trial will assess the effect of selinexor or placebo added to a standard backbone immunochemotherapy of rituximab-gemcitabine-dexamethasone-platinum, or R-GDP, in patients with one to two prior treatments for DLBCL. Selinexor has received orphan drug designation from the FDA for the DLBCL indication. We expect that the XPORT-DLBCL-030 study will begin by the end of 2020. With respect to an MAA submission to the EMA for DLBCL based on the SADAL study, we are continuing to evaluate the optimal regulatory and access strategy.

Our focus is on marketing XPOVIO in its currently approved indications as well as seeking the regulatory approval and potential commercialization of selinexor as an oral agent in additional cancer indications with significant unmet medical needs. We plan to conduct additional clinical trials and seek additional approvals for the use of selinexor in combination with other oncology therapies to expand the patient populations that are eligible to be treated with selinexor. Thus, we are currently advancing the clinical development of selinexor in multiple hematological malignancies and solid tumor indications. Ongoing clinical trials evaluating selinexor include the Phase 1b/2 STOMP (Selinexor and Backbone Treatments of Multiple Myeloma Patients) study in combination with standard therapies in multiple myeloma, the randomized Phase 2/3 SEAL (Selinexor in Advanced Liposarcoma) study evaluating single agent selinexor versus placebo in patients with previously treated, advanced unresectable dedifferentiated liposarcoma following at least two prior therapies, and the randomized Phase 3 SIENDO (Selinexor/Placebo After Combination Chemotherapy In Patients with Advanced or Recurrent Endometrial Cancer) study evaluating selinexor as maintenance therapy in endometrial cancer.

On November 2, 2020, we announced positive top-line results from the Phase 3 portion of the randomized, double blind, placebo controlled, cross-over, SEAL study. The SEAL study met its primary endpoint of a statistically significant increase in progression-free survival (hazard ratio=0.70; p=0.023). These data indicate that treatment with XPOVIO reduced the risk of disease progression or death by approximately 30%, compared to placebo. The trial allowed patients on placebo with objective progression to cross over to the XPOVIO treatment arm. Among those patients who received XPOVIO, there was a trend towards an improvement in the median overall survival compared to those patients who began on the placebo arm of the study and never crossed over to the XPOVIO treatment arm of the study. The safety profile for XPOVIO was consistent with previous clinical studies with fewer hematologic and infectious adverse events as compared to XPOVIO studies in patients with multiple myeloma and DLBCL. We expect to submit an NDA in the first quarter of 2021 requesting FDA approval of XPOVIO to treat the patient population studied in SEAL.

In April 2020, we initiated a global randomized Phase 2 clinical trial for low dose oral selinexor in hospitalized patients with severe COVID-19, or XPORT-CoV-1001. While the results of this study demonstrated encouraging anti-viral and anti-inflammatory activity in an important subset of treated patients, the interim analysis indicated that the trial was unlikely to meet its pre-specified primary endpoint across the entire patient population studied, and the trial was discontinued. Although the FDA's opinion was that the benefit-risk ratio was not favorable in the heterogenous patient population evaluated in XPORT-CoV-1001, which evaluated selinexor versus placebo in hospitalized patients with COVID-19 and included patients with more severe disease, we remain encouraged by the potential mechanistic activity of XPO1 inhibition and believe that these results warrant additional research of XPO1 inhibitors in COVID-19 and other infectious diseases.

In June 2020, the first patient was dosed in a Phase 1/2 clinical study evaluating oral selinexor in combination with standard of care therapy in patients with newly diagnosed or recurrent glioblastoma, or GBM. This global study is expected to enroll approximately 400 patients at clinical sites in the U.S., Europe, and Israel. The randomized, multi-center, Phase 1/2 study is expected to be conducted in two phases: a Phase 1 dose finding study followed by a Phase 2 randomized efficacy exploration study, designed to independently evaluate three different combination regimens in three treatment arms in patients with newly diagnosed GBM (Arms A and B) or with recurrent GBM (Arm C). Arms A and B will investigate selinexor in combination with radiation therapy with or without the addition of temozolomide, while Arm C will evaluate the combination of selinexor and lomustine. The primary endpoint of the Phase 1 study is to establish the maximum tolerated dose, and the primary endpoint of the Phase 2 study is progression-free survival in patients with newly diagnosed GBM and overall survival in patients with recurrent GBM.

In addition to selinexor, we are also advancing a pipeline of novel drug candidates including our other oral SINE compounds eltanexor and verdinexor, as well as our oral dual PAK4/NAMPT inhibitor, KPT-9274. We began clinical testing of eltanexor, a second-generation SINE compound, in late 2015. Our clinical development program for eltanexor includes myelodysplastic syndrome, or MDS, colorectal cancer and metastatic castration-resistant prostate cancer. Based on clinical results to date and resource prioritization, we are continuing to focus on the development of eltanexor in MDS. In August 2020, safety and efficacy results from a Phase 2 study of selinexor in patients with MDS or oligoblastic acute myeloid leukemia refractory to hypomethylating agents were published in *The Lancet Haematology*. Currently, no standard therapy for such patients exists. In the 23 evaluable patients, the overall response rate was 26% (95% CI 10 - 48) in six patients with marrow complete remission, with an additional 12 patients (52%, 95% CI 31 - 73) achieving stable disease. The most common grade 3 or 4 adverse events were thrombocytopenia (eight, or 32%, of 25 patients) and hyponatraemia (five, or 20%, of 25 patients). There were no drug-related serious adverse events and no treatment-related deaths. In addition, we have been evaluating KPT-9274 in patients with hematologic or solid tumors since 2016 and in July 2020, dosed the first patient in a Phase 1/2 clinical study of KPT-9274 in combination with an anti-PD1 monoclonal antibody. Finally, verdinexor is our lead compound that is being evaluated as a potential therapy for viral, rare disease and autoimmune indications in humans and by a collaborator as a potential therapy for cancers in companion animals.

In May 2020, we agreed with Antengene Therapeutics Limited, or Antengene, to an expansion of their development and commercial rights to our compounds in parts of Asia, Australia and New Zealand by entering into an amendment to the May 2018 license agreement between us and Antengene, or the Original Antengene Agreement, and as amended, the Amended Antengene Agreement. We granted Antengene, our existing partner in China and other regions in Asia, the exclusive right to develop and commercialize selinexor and eltanexor in all human oncology indications in the following geographies comprising the Antengene Territory: Australia, New Zealand, South Korea, Taiwan, Hong Kong and the countries in the Association of Southeast Asian Nations, which are currently comprised of Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, Philippines, Singapore, Thailand, and Vietnam. The Amended Antengene Agreement also includes the development and commercialization of KPT-9274 in all human oncology indications and verdinexor in human non-oncology indications in Australia and New Zealand. Under the terms of the Amended Antengene Agreement, we received a one-time upfront payment of \$11.7 million from Antengene in June 2020. We are also eligible to receive additional payments if certain future prespecified development, regulatory and commercialization milestones are achieved by Antengene. In addition, we are also eligible to receive tiered double-digit royalties based on future net sales of selinexor and eltanexor, and tiered single- to double-digit royalties based on future net sales of verdinexor and KPT-9274 in the Antengene Territory. Certain countries in the Antengene Territory became available due to the reacquisition of exclusive development and commercial rights from Ono Pharmaceutical Co., Ltd. in April 2020.

As of September 30, 2020, we had an accumulated deficit of \$1.0 billion. We had net losses of \$152.9 million and \$150.9 million for the nine months ended September 30, 2020 and 2019, respectively. As of September 30, 2020, we have generated \$86.5 million to date in net product sales from XPOVIO, which first became commercially available in the U.S. in July 2019.

Commercialization of XPOVIO in the United States

The commercialization of XPOVIO, for both the multiple myeloma and the DLBCL indications, is being supported by approximately 70 sales representatives and nurse liaisons as well as KaryForward™, an extensive patient and healthcare provider support program. Our commercial efforts are also being supplemented by patient support initiatives coordinated by our dedicated network of participating specialty pharmacy providers.

As of September 30, 2020, nearly 4,200 XPOVIO prescriptions have been filled since launch, driven by strong demand from both academic and community-based physicians. Net product sales for XPOVIO were \$56.0 million and \$12.8 million for the nine months ended September 30, 2020 and 2019, respectively.

We plan to continue to build upon XPOVIO's early commercial success in the late-line relapsed or refractory multiple myeloma market by continuing to educate physicians, healthcare providers and patients about XPOVIO's clinical profile and unique mechanism of action. Based on the positive results from the BOSTON trial, which we announced in early March 2020, our commercial team is preparing for XPOVIO's potential expansion into the second line multiple myeloma market, subject to the FDA's review and approval of our sNDA based on the data from the BOSTON trial, which has been assigned a March 19, 2021 PDUFA date.

Commercialization Outside of the United States

In January 2019, based on the results of the Phase 2b STORM study, we submitted an MAA to the EMA requesting conditional approval for selinexor in combination with dexamethasone as a treatment for patients with triple class refractory multiple myeloma, meaning patients who have received at least three prior therapies and whose disease is refractory to at least one PI, one IMiD, and one anti-CD38 monoclonal antibody. In 2019, we received feedback from EMA's Committee for Medicinal Products for Human Use, or CHMP, including an integrated inspection report, based on site audits and a sponsor inspection. In January 2020, we were granted a three-month extension from CHMP to provide additional time to respond to the CHMP's outstanding questions related to the application. In September 2020, we submitted our responses following an additional extension of time due to the impact of the COVID-19 pandemic. In October 2020, we received a further updated list of outstanding issues, or LOI, from CHMP summarizing the remaining topics for us to address and indicating that, as part of its assessment of the safety and efficacy of selinexor based on the STORM study, the CHMP intends to consult its Scientific Advisory Group for additional advice in the fourth quarter of 2020. The LOI indicates that the CHMP is continuing to assess the Independent Review Committee's adjudicated responses from the STORM study and asks us to justify the positive benefit-risk in the intended indication, which CHMP has also requested that we update to be more closely aligned with the patient population evaluated in the STORM study. The LOI further requests that we demonstrate that selinexor provides an advantage over approved therapies in the relevant indication and that we provide a summary of top-line data from the BOSTON study and the context of such data for the current application. We are currently in the process of preparing responses to the LOI, and we continue to expect to receive an opinion from CHMP with respect to this MAA before the end of 2020. In addition, contingent upon and following receipt of CHMP's opinion, we plan to submit an MAA before the end of 2020 with a request for conditional approval of selinexor in combination with Velcade® (bortezomib) and low-dose dexamethasone in patients with multiple myeloma after at least one prior line of therapy based on data from our BOSTON study.

To commercialize selinexor following any regulatory approval outside of the U.S., we will work with existing and potential future partners to establish the appropriate commercial infrastructure outside of the U.S., or we may, in certain geographies, elect to establish the commercial infrastructure ourselves. We maintain complete commercial rights to selinexor in all territories outside of the Antengene Territory and Israel, including the U.S., Canada, Europe, Japan, and Latin America.

Uncertainty Relating to the COVID-19 Pandemic

The COVID-19 pandemic has and will continue to affect economies and businesses around the world. We are closely monitoring the impact of the COVID-19 pandemic on all aspects of our business, including the impact on our employees, patients and business operations. We have and may continue to experience disruptions in the future that could impact our results of operations and financial condition. Although we do not currently expect that the ongoing COVID-19 pandemic will have a material impact on our business plans or results of operations, we are unable to predict the impact that the COVID-19 pandemic will have on our operating results and financial condition due to numerous uncertainties. These uncertainties include the geographic spread of the pandemic, the severity of the virus, the duration of the outbreak, governmental, business or other actions, travel restrictions and social distancing, business closures or business disruptions, or changes to our operations, among others. We will continue to monitor the COVID-19 situation closely and intend to follow health and safety guidelines as they evolve. Further, the impacts of a potential worsening of global economic conditions and the continued disruptions to, and volatility in, the credit and financial markets, as well as other unanticipated consequences remain unknown. The situation surrounding the COVID-19 pandemic remains fluid and continues to rapidly evolve, and we are actively managing our response and assessing potential impacts to our operating results and financial condition, as well as adverse developments in our business. For further information regarding the impact of the COVID-19 pandemic on us, see Item 1A - Risk Factors included in this Quarterly Report on Form 10-Q.

CRITICAL ACCOUNTING POLICIES AND SIGNIFICANT JUDGMENTS AND 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 were no changes to the critical accounting policies we identified in our Annual Report. It is important that the discussion of our operating results that follows be read in conjunction with the critical accounting policies disclosed in our Annual Report.

RESULTS OF OPERATIONS

Comparison of the Three Months Ended September 30, 2020 and September 30, 2019

	For the Three Months Ended September 30,		\$ Change	% Change
	2020	2019		
	(in thousands)			
Product revenue, net	\$ 21,330	\$ 12,821	\$ 8,509	66%
License and other revenue	3	328	(325)	(99)%
Operating expenses:				
Cost of sales	438	1,013	(575)	(57)%
Research and development	37,037	26,270	10,767	41%
Selling, general and administrative	30,967	25,267	5,700	23%
Loss from operations	(47,109)	(39,401)	(7,708)	20%
Other expense, net	(6,342)	(1,946)	(4,396)	226%
Loss before income taxes	(53,451)	(41,347)	(12,104)	29%
Income tax provision	(44)	(20)	(24)	120%
Net loss	\$ (53,495)	\$ (41,367)	\$ (12,128)	29%

Product revenue, net. We recognized \$21.3 million and \$12.8 million of net product revenue in the three months ended September 30, 2020 and 2019, respectively, from U.S. commercial sales of XPOVIO. We began to record net product revenue in the third quarter of 2019 following the July 2019 FDA approval of XPOVIO and its subsequent commercial launch in the U.S.

License and other revenue. We recognized an insignificant amount of license and other revenue for the three months ended September 30, 2020 and \$0.3 million of license and other revenue for the three months ended September 30, 2019. We expect license and other revenue to increase slightly in the fourth quarter.

Cost of sales. Cost of sales includes the cost of producing and distributing inventories that are related to U.S. XPOVIO product revenue during the respective period (including salary-related and stock-based compensation expenses for employees involved with XPOVIO production and distribution) and third-party royalties payable on our net product revenue for XPOVIO. We began capitalizing XPOVIO inventory costs during the third quarter of 2019 subsequent to FDA approval, as our expectation was that such costs will be recoverable through commercialization of XPOVIO. Prior to the capitalization of XPOVIO inventory costs, such costs were recorded as research and development expenses in the period incurred. During the three months ended September 30, 2020 and 2019, we recorded \$0.4 million and \$1.0 million, respectively, of cost of sales, including \$0.1 million and \$0.7 million, respectively, related to royalties. The cost of sales during the three months ended September 30, 2020 and 2019 only reflects a portion of the costs related to the manufacturing of XPOVIO and related materials, since, prior to FDA approval, these costs were expensed. The manufacturing costs of XPOVIO on-hand upon FDA approval amounted to approximately \$2.8 million. At September 30, 2020, we had \$2.1 million of this previously expensed XPOVIO and related material on-hand. We expect to utilize zero cost inventory with respect to XPOVIO for an extended period of time.

We expect cost of sales to remain relatively consistent in the fourth quarter compared to the third quarter.

Research and development expense. Research and development expense increased approximately \$10.7 million to \$37.0 million for the three months ended September 30, 2020 from approximately \$26.3 million for the three months ended September 30, 2019. The increase was primarily related to:

- an increase of \$7.0 million in clinical trial costs, primarily related to COVID-19 trial activity as well as continued activity in our ongoing clinical trials;
- an increase of \$3.4 million in personnel costs, primarily related to an increase in headcount; and
- an increase of \$0.9 million in facility and IT infrastructure costs; partially offset by
- a decrease of \$0.6 million in travel, consulting and professional costs.

We expect our research and development expense to remain relatively consistent in the fourth quarter when compared to the third quarter, with possible fluctuation due to timing of clinical trial study starts and related clinical trial enrollment.

Selling, general and administrative expense. Selling, general and administrative expense increased approximately \$5.7 million to \$31.0 million for the three months ended September 30, 2020 from approximately \$25.3 million for the three months ended September 30, 2019. The increase was primarily related to:

- an increase of \$3.9 million in personnel costs, primarily related to an increase in headcount;
- an increase of \$2.8 million in commercial-related activities; and
- an increase of \$0.1 million in facility and IT infrastructure costs; partially offset by
- a decrease of \$1.1 million in travel, consulting and professional costs.

We expect our selling, general and administrative expenses to remain relatively consistent in the fourth quarter when compared to the third quarter as a result of decreased travel and corporate events due to COVID-19 impacts, offset by costs expected to be incurred in anticipation of the launch, if approved, of the expanded indication for XPOVIO, based on the BOSTON study, to treat patients with multiple myeloma after at least one prior line of therapy.

Other expense, net. Other expense, net increased from \$1.9 million for the three months ended September 30, 2019 to \$6.3 million for the three months ended September 30, 2020. The net increase of approximately \$4.4 million was primarily due to an increase in interest expense of \$3.7 million, coupled with a decrease in interest income of \$0.5 million. Of the \$3.7 million increase in interest expense, \$3.4 million was related to our Revenue Interest Financing Agreement, or deferred royalty obligation, and \$0.3 million was related to our 3.00% senior convertible notes due 2025, or Notes.

We expect interest expense to increase slightly in the fourth quarter when compared to the third quarter, related to the imputed interest on our deferred royalty obligation.

Comparison of the nine months ended September 30, 2020 and September 30, 2019

	Nine Months Ended September 30,		\$ Change	% Change
	2020	2019		
	(in thousands)			
Product revenue, net	\$ 55,992	\$ 12,821	\$ 43,171	337%
License and other revenue	16,993	9,976	7,017	70%
Operating expenses:				
Cost of sales	1,653	1,013	640	63%
Research and development	113,628	90,761	22,867	25%
Selling, general and administrative	92,488	77,032	15,456	20%
Loss from operations	(134,784)	(146,009)	11,225	(8)%
Other expense, net	(17,821)	(4,896)	(12,925)	264%
Loss before income taxes	(152,605)	(150,905)	(1,700)	1%
Income tax provision	(247)	(38)	(209)	550%
Net loss	\$ (152,852)	\$ (150,943)	\$ (1,909)	1%

Product revenue, net. We recognized \$56.0 million and \$12.8 million of net product revenue in the nine months ended September 30, 2020 and 2019, respectively, from U.S. commercial sales of XPOVIO. We began to record net product revenue in the third quarter of 2019 following the 2019 FDA approval of XPOVIO and its subsequent commercial launch in the U.S. We did not generate any revenue from product sales prior to July 2019.

License and other revenue. License and other revenue for the nine months ended September 30, 2020 was \$17.0 million compared to \$10.0 million for the nine months ended September 30, 2019. During the nine months ended September 30, 2020, we recognized \$13.8 million pursuant to the Antengene Agreement, \$2.2 million upon reacquisition of the exclusive development and commercial rights from Ono, and \$1.0 million related to clinical supply provided to various partners, as well as grant revenue pursuant to a government grant arrangement. During the nine months ended September 30, 2019, we recognized \$9.4 million in revenue pursuant to the Original Antengene Agreement, \$0.2 million in revenue for clinical supply provided to various partners, and \$0.3 million in grant revenue pursuant to a government grant arrangement.

Cost of sales. During the nine months ended September 30, 2020 and 2019, we recorded \$1.7 million and \$1.0 million, respectively, of cost of sales, including \$1.0 million and \$0.7 million, respectively, related to royalties.

Research and development expense. Research and development expense increased approximately \$22.8 million to \$113.6 million for the nine months ended September 30, 2020 from approximately \$90.8 million for the nine months ended September 30, 2019. The increase was primarily related to:

- an increase of \$12.7 million in clinical trial costs, primarily related to COVID-19 trial activity as well as continued activity in our ongoing clinical trials;
- an increase of \$9.5 million in personnel costs, primarily related to an increase in headcount; and
- an increase of \$2.6 million in facility and IT infrastructure costs; partially offset by
- a decrease of \$2.0 million in travel, consulting and professional costs.

Selling, general and administrative expense. Selling, general and administrative expense increased approximately \$15.5 million to \$92.5 million for the nine months ended September 30, 2020 from approximately \$77.0 million for the nine months ended September 30, 2019. The increase was primarily related to:

- an increase of \$10.3 million in commercial-related activities;
- an increase of \$8.2 million in personnel costs, primarily related to an increase in headcount; and
- an increase of \$0.5 million in facility and IT infrastructure costs; partially offset by
- a decrease of \$3.5 million in travel, consulting and professional costs.

Other expense, net. Other expense, net increased from \$4.9 million for the nine months ended September 30, 2019 to \$17.8 million for the nine months ended September 30, 2020. The increase of approximately \$12.9 million was primarily due to an increase in interest expense of \$10.9 million, coupled with a decrease in interest income of \$2.0 million. \$10.2 million of the increase in interest expense was related to our deferred royalty obligation and \$0.7 million of the increase was attributable to our Notes.

LIQUIDITY AND CAPITAL RESOURCES

Sources of Liquidity

During the third quarter of 2019, we began generating revenues from product sales, as XPOVIO first became commercially available in the U.S. in July 2019. We have had limited revenues to date from product sales and have financed our operations principally through private placements of our preferred stock, proceeds from our initial public offering and follow-on offerings of common stock, proceeds from the issuance of convertible debt, proceeds pursuant to the deferred royalty obligation, and cash generated from our business development activities. Although we do not currently expect that the ongoing COVID-19 pandemic will have a material impact on our business plans or results of operations, we are continually monitoring our liquidity and capital requirements in light of the evolving situation.

At September 30, 2020, our principal source of liquidity was \$302.4 million of cash, cash equivalents and investments. We have had recurring losses and incurred a loss of \$152.9 million for the nine months ended September 30, 2020. Net cash used in operations for the nine months ended September 30, 2020 was \$129.6 million. We expect that our cash, cash equivalents and investments at September 30, 2020 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.

On May 5, 2020, we entered into Amendment No. 1 to the Open Market Sale Agreement, dated August 17, 2018, or the Open Market Sale Agreement, with Jefferies LLC, as agent, or Jefferies, pursuant to which we increased the maximum aggregate offering price of shares of our common stock that we may issue and sell from time to time through Jefferies, by \$100.0 million from \$75.0 million to up to \$175.0 million. We did not sell any shares under the Open Market Sale Agreement during the third quarter of 2020. As of October 30, 2020, we have sold an aggregate of 3,712,359 shares under the Open Market Sale Agreement, for net proceeds of approximately \$46.2 million, all of which were sold in 2019.

On March 6, 2020, we completed a follow-on offering under our shelf registration statement on Form S-3 pursuant to which we issued an aggregate of 7,187,500 shares of common stock, which included the full exercise of the underwriters' option to purchase additional shares, at a public offering price of \$24.00 per share. We received aggregate net proceeds of approximately \$161.8 million from the offering after deducting the underwriting discounts and commissions and other offering expenses.

On September 14, 2019, we entered into a deferred royalty obligation, with HealthCare Royalty Partners III, L.P. and HealthCare Royalty Partners IV, L.P. or HCR. Pursuant to the deferred royalty obligation, HCR paid us \$75.0 million, less certain transaction expenses, at the initial closing, which occurred on September 27, 2019, as disclosed in Note 11 to the Condensed Consolidated Financial Statements included under Part I, Item 1 of this Quarterly Report on Form 10-Q.

Cash Flows

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

	Nine Months Ended September 30,	
	2020	2019
Net cash used in operating activities	\$ (129,600)	\$ (151,333)
Net cash (used in) provided by investing activities	(85,082)	111,969
Net cash provided by financing activities	168,115	89,369
Effect of exchange rate changes	(15)	(26)
Net (decrease) increase in cash, cash equivalents and restricted cash	<u>\$ (46,582)</u>	<u>\$ 49,979</u>

Operating activities. The net cash used in operating activities in both periods resulted primarily from our net losses adjusted for non-cash charges and changes in the components of working capital. The decrease in cash used in operating activities during the nine months ended September 30, 2020, compared to the nine months ended September 30, 2019, was primarily driven by our decreased loss from operations during that period.

Investing activities. The net cash (used in) provided by investing activities during the nine months ended September 30, 2020, compared to the nine months ended September 30, 2019, primarily reflects a \$157.6 million increase in the purchases of investments, coupled with a \$39.6 million decrease in proceeds from the maturities of investments.

Financing activities. The net cash provided by financing activities for the nine months ended September 30, 2020, compared to the nine months ended September 30, 2019, reflects an increase of \$78.7 million. The increase was primarily related to the net cash proceeds of \$161.8 million from the sale of shares of our common stock from the follow-on offering under our shelf registration statement on Form S-3 during the first quarter of 2020, coupled with a \$5.2 million increase in proceeds from the exercise of stock options and shares issued under our Employee Stock Purchase Program in the first nine months of 2020 compared to the first nine months of 2019, partially offset by the \$73.7 million net proceeds received in the third quarter of 2019 from the execution of our deferred royalty obligation in the third quarter of 2019.

Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue to commercialize XPOVIO and continue the clinical trials of, and as we seek marketing approval for, our drug candidates. In addition, we expect to incur significant commercialization expenses related to sales, marketing, manufacturing and distribution of any of our drug candidates for which we obtain marketing approval, to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of any collaborator that we may have at such time for any such drug candidate. Furthermore, we expect to continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. 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.

Our future capital requirements will depend on many factors, including:

- revenue generated from commercial sales of XPOVIO;
- costs related to the sales and marketing of XPOVIO;
- the costs, timing and outcome of regulatory review of our drug candidates;
- the costs of future commercialization activities, including drug sales, marketing, manufacturing and distribution, for any of our drug candidates for which we receive marketing approval, to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of any collaborator that we may have at such time;
- the amount of revenue received from commercial sales of our drug candidates for which we receive marketing approval;
- the progress and results of our current and planned clinical trials of selinexor;

- the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our other drug candidates;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the success of any collaborations that we may enter into with third parties;
- the extent to which we acquire or in-license other drugs and technologies;
- the costs associated with legal activities, including litigation, arising in the course of business activities and our ability to prevail in any such legal disputes; and
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims.

Identifying potential drug candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete. In addition, our drug 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. While we began to generate revenue from the sales of XPOVIO in July 2019, 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. 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.

OFF-BALANCE SHEET ARRANGEMENTS

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under SEC rules.

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 \$302.4 million as of September 30, 2020. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because the majority of our investments are in short-term securities. 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, restricted cash 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 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 Chief Executive Officer (principal executive officer) and Senior Vice President, Chief Financial Officer and Treasurer (principal financial officer), evaluated the effectiveness of our disclosure controls and procedures as of September 30, 2020. 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 September 30, 2020, our Chief Executive Officer and our Senior 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 September 30, 2020 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 1. Legal Proceedings.

We have been named as a defendant in a securities class action litigation filed on July 23, 2019, in the U.S. District Court for the District of Massachusetts. The complaint was filed by the Allegheny County Employees' Retirement System, against us and certain of our current and former executive officers and directors as well as the underwriters of our public offerings of common stock conducted in April 2017 and May 2018. This complaint was voluntarily dismissed on March 12, 2020. A second complaint was filed by Heather Mehdi on September 17, 2019, in the same court and against the same defendants with the exception of the underwriters. In April 2020, the court appointed a lead plaintiff, Myo Thant ("Plaintiff"), who filed an amended complaint on June 29, 2020. The amended complaint alleges violations of federal securities laws based on our disclosures related to the results from the Phase 2 SOPRA study and Part 2 of the Phase 2b STORM study, and seeks unspecified compensatory damages, including interest; reasonable costs and expenses, including attorneys' and expert fees; and such equitable/injunctive relief or other relief as the court may deem just and proper. We have reviewed the allegations and believe they are without merit. We moved to dismiss the complaint on July 31, 2020 and concluded related briefing in September 2020. Before the court ruled on this motion to dismiss, Plaintiff filed a second amended complaint. We moved to dismiss the second amended complaint on November 2, 2020. We intend to defend vigorously against this litigation.

Item 1A. Risk Factors.

Careful consideration should be given to the following 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, or 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.

Risks Related to the Discovery, Development and Commercialization of Our Drugs and Drug Candidates

The COVID-19 pandemic has adversely disrupted, and is expected to continue to adversely disrupt, our operations, including our clinical trial activities and commercial operations, which could have an adverse effect on our business and financial results.

The outbreak of the novel coronavirus disease, or COVID-19, is a global pandemic that has affected many segments of the global economy. As a result, we have experienced, and we expect to continue to experience, disruptions that could adversely impact our business, clinical trial activities and commercial operations, including:

- negative impact to revenue for XPOVIO® (selinexor) tablets, which may continue as the COVID-19 pandemic persists, including as a result of decreased new patient starts due to the inability of our sales force and our patients to meet with healthcare professionals;
- delays or difficulties in enrolling patients in our clinical trials, including our SIENDO and STOMP trials;
- delays or difficulties in initiating new clinical studies, including clinical site initiation and difficulties in recruiting clinical site investigators and clinical site staff;
- reduction or diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by government officials or entities, employers and others or interruption of clinical trial patient visits and study procedures (particularly any procedures that may be deemed non-essential), which may impact the integrity of clinical trial data and clinical study endpoints;
- interruption or delays in the operations of the U.S. Food and Drug Administration, or FDA, and comparable foreign regulatory agencies, including the European Medicines Agency, or EMA, which may impact regulatory review and approval timelines, such as the EMA review of our Marketing Authorization Application, or MAA, for selinexor in multiple myeloma based on the results on the STORM study and any resulting impact to the timing of our expected submission of an MAA for selinexor in multiple myeloma supported by the results of the BOSTON study or any future MAA submission;
- negative impacts on any or all aspects of our operations due to business disruptions related to COVID-19 at our third-party vendors who we rely upon in the conduct of our business; and

- limitations on employee resources that would otherwise be focused on the conduct of our business, including because of sickness of employees or their families, the desire of employees to avoid contact with large groups of people, and an increased reliance on working from home.

The COVID-19 pandemic continues to evolve, and its ultimate scope, duration and effects are unknown. The extent of the impact of the disruptions to our business, including commercial sales and clinical trials, as a result of the pandemic will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the pandemic, travel restrictions and actions to contain the pandemic or treat its impact, including social distancing and quarantines or lock-downs in the U.S. and other countries, business closures or business disruptions and the effectiveness of actions taken in the U.S. and other countries to contain and treat the disease.

We depend heavily on the success of XPOVIO. If we are unable to successfully commercialize our current and future indications of XPOVIO or successfully develop our other drug candidates within or outside of the U.S., or if we experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the research and development of our lead drug, selinexor. In July 2019, the FDA granted accelerated approval for XPOVIO 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, or the multiple myeloma indication. In June 2020, the FDA granted accelerated approval for XPOVIO for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma, or DLBCL, not otherwise specified, including DLBCL arising from follicular lymphoma, after at least two lines of systemic therapy, or the DLBCL indication. Our ability to generate revenues from the sale of drugs that treat cancer and other diseases in humans will depend heavily on the successful development, additional regulatory approvals and commercialization of selinexor.

The commercial success of our current and future indications of XPOVIO and the successful clinical development of our other drug candidates will depend on several factors, including the following:

- our ability to successfully launch our approved products, including the recently approved DLBCL indication for XPOVIO, or any drug candidates for which we obtain marketing approval, whether alone or in collaboration with others;
- 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 FDA accelerated approvals and/or FDA package insert for XPOVIO;
- our ability to comply with FDA post-marketing requirements and commitments, including through successfully conducting additional studies that confirm clinical efficacy, effectiveness and safety of XPOVIO and acceptance of the same by the FDA and the medical community since continued approval for our current indications may be contingent upon verification of a clinical benefit in confirmatory trials;
- acceptance of our current and future indications of XPOVIO and, if and when approved, our other drug candidates, 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 drug candidates, if approved;
- successful and timely completion of preclinical studies;
- acceptance by the FDA of investigational new drug applications, or INDs, for our drug candidates prior to commencing clinical studies;
- successful and timely enrollment in, and completion of, clinical trials, including demonstration of a favorable risk-benefit ratio;
- receipt of marketing approvals from applicable regulatory authorities in a timely fashion;
- establishing and maintaining commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our drugs and drug candidates;
- establishing and maintaining sales, marketing, manufacturing and distribution capabilities to commercialize our currently approved drugs and any drug candidates for which we obtain marketing approval, whether alone or in collaboration with others;
- effectively competing with other therapies;

- maintaining an acceptable safety profile of our approved drugs;
- compliance with existing and new health care laws and regulations currently being considered or implemented in the U.S., including government pricing, price reporting and other disclosure requirements related to such laws and regulations and the potential impact of such requirements on physician prescribing practices and payor coverage;
- enforcing and defending intellectual property rights and claims;
- maintaining and growing an organization of scientists and business people, including collaborators, who can develop and commercialize our drug candidates; and
- the impact of the COVID-19 pandemic on the above factors, including the limitation of our sales professionals to meet with healthcare professionals as the result of travel restrictions or hospital limitations on access for non-patients.

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

The results of previous clinical trials may not be predictive of future results and the results of our current and planned clinical trials may not satisfy the requirements of the FDA or non-U.S. regulatory authorities.

Clinical failure can occur at any stage of the clinical development process. Clinical trials may produce negative or inconclusive results, and we or any collaborators may decide, or regulators may require us, to conduct additional clinical trials or preclinical studies. We will be required to demonstrate with substantial evidence through well-controlled clinical trials that our drug candidates are safe and effective for use in a diverse population before we can seek regulatory approvals for their commercial sale. Success in early-stage clinical trials does not mean that future larger registration clinical trials will be successful because drug candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA and non-U.S. regulatory authorities despite having progressed through early-stage clinical trials. Drug candidates that have shown promising results in early-stage clinical trials may still suffer significant setbacks in subsequent registration clinical trials. Additionally, interim results of a clinical trial are not necessarily indicative of final results.

In addition, the design of a clinical trial can determine whether its results will support approval of a drug, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We may be unable to design and conduct a clinical trial to support regulatory approval. Further, if our drug candidates are found to be unsafe or lack efficacy, we will not be able to obtain regulatory approval for them and our business would be harmed. A number of companies in the pharmaceutical industry, including those with greater resources and experience than us, have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier clinical trials.

In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same drug candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, 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 sufficient to obtain regulatory approval to market our drug candidates.

Further, our drug candidates may not be approved even if they achieve their primary endpoints in Phase 3 clinical trials or other registration trials. The FDA or non-U.S. regulatory authorities may disagree with our trial design and our interpretation of data from preclinical studies and clinical trials. For example, on November 2, 2020, we announced top-line data from the Phase 3 portion of the randomized, double blind, placebo controlled, cross-over SEAL study of selinexor versus placebo in advanced unresectable dedifferentiated liposarcoma following at least two prior therapies. Although we believe these data are positive, top-line data includes certain assumptions, estimations, calculations and conclusions as part of our analyses of the top-line data and the data remains subject to audit and verification procedures that may cause final data to differ, even materially. If the FDA, or other regulatory authorities, disagree about the overall benefit-risk assessment and data analyses, we may not obtain approval for XPOVIO to treat advanced unresectable dedifferentiated liposarcoma, which could harm our business, financial condition, results of operations and prospects, including our ability to advance our solid tumor programs for selinexor.

In addition, any of these regulatory authorities may change the requirements for the approval of a drug candidate even after providing a positive opinion on, or otherwise reviewing and providing comments or advice on, a protocol for a clinical trial that has the potential to result in approval by the FDA or another regulatory authority. In addition, any of these regulatory authorities may also approve a drug candidate for fewer or more limited indications than we request or may grant approval contingent on the performance of costly post-marketing clinical trials. Furthermore, the FDA or non-U.S. regulatory authorities may not approve the labeling claims that we believe would be necessary or desirable for the successful commercialization of our drug candidates.

To date, we have had several discussions with the FDA and non-U.S. regulatory authorities regarding the design of our later phase clinical trials for selinexor, including the BOSTON, STORM, SADAL and SEAL studies. In July 2019 and June 2020, the FDA approved the multiple myeloma indication and the DLBCL indication, respectively, under its Accelerated Approval program based on response rate from the STORM and SADAL studies, respectively. We plan to seek additional regulatory approvals of selinexor in North America and Europe in each indication with respect to which such later phase clinical trial is being conducted and with respect to which we receive positive results that may support full or accelerated approval, as the case may be. We or our current or future partners may also seek such approvals in other geographies. We cannot be certain that we will commence additional later phase trials or complete ongoing later phase trials as anticipated. Before obtaining regulatory approvals for the commercial sale of any drug candidate for a target indication, we must demonstrate with substantial evidence gathered in preclinical studies and well-controlled clinical studies, and, with respect to approval in the U.S., to the satisfaction of the FDA, that the drug candidate is safe and effective for use for that target indication. There is no assurance that the FDA or non-U.S. regulatory authorities would consider our current and planned later phase clinical trials to be sufficient to serve as the basis for filing for approval or to gain approval of selinexor for any indication. The FDA and non-U.S. regulatory authorities retain broad discretion in evaluating the results of our clinical trials and in determining whether the results demonstrate that selinexor or any of our other drug candidates is safe and effective. If we are required to conduct additional clinical trials of selinexor or our other drug 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 results to date in preclinical and early clinical studies conducted by us or our academic collaborators and in Phase 1 and Phase 2 clinical trials that we are currently conducting include the response of tumors to selinexor. We expect that in any later phase clinical trial where patients are randomized to receive either selinexor on the one hand, or standard of care, supportive care or placebo on the other hand, the primary endpoint will be either progression-free survival, meaning the length of time on treatment until objective tumor progression, or overall survival, while the primary endpoint in any later phase clinical trial that is not similarly randomized may be different. For example, the primary endpoint of our Phase 2/3 SEAL study, the clinical trial of selinexor in patients with dedifferentiated liposarcoma, and of our Phase 3 BOSTON study, the clinical trial of selinexor in combination with Velcade (bortezomib) and dexamethasone in patients with multiple myeloma, is progression-free survival. In some instances, the FDA and other regulatory bodies have accepted overall response rate as a surrogate for a clinical benefit and have granted regulatory approvals based on this or other surrogate endpoints. Overall response rate is defined as the portion of patients with tumor size reduction of a predefined amount for a minimum time period. For some types of cancer, we may use overall response rate as a primary endpoint, as we did in our SADAL study and our STORM study. These clinical trials were not randomized against control arms and the primary endpoints of these trials were overall response rate. If selinexor does not demonstrate sufficient overall response rates for any other indication for which a clinical trial has overall response rate as a primary endpoint, or if the FDA or non-U.S. regulatory authorities do not deem overall response rate a sufficient endpoint, or deem a positive overall response rate to be insufficient, selinexor will likely not be approved for that indication based on the applicable study.

Finally, independent review committees are typically implemented to adjudicate efficacy outcomes in clinical studies that are intended to support requests for regulatory approval. For example, in our STORM study, the primary endpoint of overall response rate was determined based on efficacy adjudications by an independent review committee, or IRC, comprised of physicians who are expert in treating and evaluating patients with multiple myeloma. While the FDA agreed with the assessments of the IRC for the STORM study in conducting its review of those data, we cannot be certain that the European Union and other regulatory authorities will agree with the assessments of the IRC for STORM or any other study for which we may submit data to support a request for regulatory approval.

We may not be successful in our efforts to identify or discover additional potential drug candidates.

Part of our strategy involves identifying and developing drug candidates to build a pipeline of novel drug 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 drug candidates, yet fail to yield drug candidates for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential drug candidates;
- potential drug 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 drug candidates may not be effective in treating their targeted diseases.

Research programs to identify new drug candidates require substantial technical, financial and human resources. We may choose to focus our efforts and resources on a potential drug candidate that ultimately proves to be unsuccessful. If we are unable to identify suitable compounds for preclinical and clinical development, we will not be able to generate revenues from the sale of drugs in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

Clinical drug development is a lengthy and expensive process, with an uncertain outcome. If clinical trials of our drug candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such drug candidates.

Before obtaining marketing approval from regulatory authorities for the sale of our drug candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later stage clinical trials, and interim results of a clinical trial do not necessarily predict final results. For example, certain data from our Phase 1 and Phase 2 clinical trials of selinexor are based on unaudited data provided by our clinical trial investigators. An audit of this data may change the conclusions drawn from this unaudited data provided by our clinical trial investigators indicating less promising results than we currently anticipate. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their drug candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their drug candidates. Furthermore, the failure of any drug candidates to demonstrate safety and efficacy in any clinical trial could negatively impact the perception of XPOVIO or our other drug candidates and/or cause the FDA or other regulatory authorities to require additional testing before any of our drug candidates are approved.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our drug candidates, including:

- delays associated with the COVID-19 pandemic, including impacts to healthcare systems, our trial sites' ability to conduct trials, and interruption or unavailability of clinical supplies, regulatory reviews, site monitors and patient enrollment;
- regulatory authorities or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- delays in reaching or failing to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites or contract research organizations;
- clinical trials of our drug candidates may produce negative or inconclusive results, and we may decide, or regulatory authorities may require us, to conduct additional clinical trials, suspend ongoing clinical trials or abandon drug development programs;
- the number of patients required for clinical trials of our drug candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors, including those manufacturing our drug candidates or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we or our investigators might have to suspend or terminate clinical trials of our drug candidates for various reasons, including non-compliance with regulatory requirements, a finding that our drug candidates have undesirable side effects or other unexpected characteristics, or a finding that the participants are being exposed to unacceptable health risks;
- regulators may recommend or require us to perform additional or unanticipated clinical trials to obtain approval;
- regulators may revise the requirements for approving our drug candidates, or such requirements may not be as we anticipate;
- the cost of clinical trials of our drug candidates may be greater than we anticipate;
- the supply or quality of our drug candidates or other materials necessary to conduct clinical trials of our drug candidates may be insufficient or inadequate; and
- any partners and collaborators that help 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.

As we seek to advance our clinical programs, we remain in close contact with our contract research organizations, clinical sites and suppliers to attempt to assess the impacts that the COVID-19 pandemic has had and may continue to have on our clinical trials, current timelines and costs and to consider whether we can implement appropriate mitigating measures to help to lessen such impacts. At this time, however, we cannot fully forecast the scope of impacts that the COVID-19 pandemic may have on our ability to initiate trial sites, enroll and assess patients, supply study drug and report trial results. To date, we have incurred delays in enrollment for our SEAL, SIENDO and STOMP clinical trials. In addition, we have and may continue to experience delays in certain regulatory filings, which may impact our approval timelines, such as the EMA review of our MAA for selinexor in multiple myeloma based on the results on the STORM study and any resulting impact to the timing of our expected submission of an MAA for selinexor in multiple myeloma supported by the results of the BOSTON study or any future MAA submission. Further, in response to the COVID-19 pandemic, the FDA issued guidance on March 18, 2020, and updated it on July 2, 2020, to address the conduct of clinical trials during the pandemic. The guidance sets out a number of considerations for sponsors of clinical trials impacted by the pandemic, including the requirement to include in the clinical study report (or as a separate document) contingency measures implemented to manage the study, and any disruption of the study as a result of COVID-19; a list of all study participants affected by COVID-19-related study disruption by unique subject identifier and by investigational site, and a description of how the individual's participation was altered; and analyses and corresponding discussions that address the impact of implemented contingency measures (e.g., participant discontinuation from investigational product and/or study, alternative procedures used to collect critical safety and/or efficacy data) on the safety and efficacy results reported for the study.

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

- be delayed in obtaining marketing approval for our drug candidates;
- not obtain marketing approval at all;
- 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; or
- have the drug removed from the market after obtaining marketing approval.

Our drug development costs will also increase if we experience delays in testing or marketing approvals. 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, particularly as a result of the COVID-19 pandemic. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our drug candidates, allow our competitors to bring drugs to market before we do or impair our ability to successfully commercialize our drug candidates, 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 drug candidates.

If we experience delays or difficulties in the enrollment of patients in clinical trials, or we are otherwise delayed in our ability to conduct clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our drug candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside of the U.S. In addition, some of our competitors may have ongoing clinical trials for drug candidates that treat the same indications as our drug candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' drug candidates.

Patient enrollment is affected by other factors, including:

- potential disruptions caused by the COVID-19 pandemic, including difficulties in initiating clinical sites or enrolling participants, diversion of healthcare resources away from clinical trials, travel or quarantine policies, and other factors;
- severity of the disease under investigation;
- availability and efficacy of approved drugs for the disease under investigation;
- patient eligibility criteria for the study in question;
- competing drugs in clinical development;

- actual or perceived risks and benefits of the drug candidate under study;
- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;
- external negative impacts to our efforts to facilitate timely enrollment in clinical trials, such as the ongoing governmental “stay at home” or “safer at home” orders related to the COVID-19 pandemic;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

In addition, patient enrollment may be affected by future regulatory actions, such as Form 483 observations or clinical holds. For example, in February 2017, following the conclusion of a joint inspection conducted by the FDA and Danish Medicines Agency at our corporate headquarters, the FDA issued a Form 483 noting certain deficiencies in procedures and documentation that were identified in our selinexor development program. In addition, in March 2017, the FDA notified us that it had placed the clinical trials under our IND for selinexor on partial clinical hold, which is an order by the FDA to delay or suspend part of a sponsor’s clinical work requested under its IND as well as investigator-sponsored trials. If in the future we are delayed in addressing, or unable to address, any concerns of the FDA or other regulators, we could be subject to other Form 483 observations or clinical holds and consequently be delayed or prevented from enrolling patients in our current or future clinical trials.

Our inability to enroll a sufficient number of patients for our clinical trials could result in significant delays, could require us to abandon one or more clinical trials altogether and could delay or prevent our receipt of necessary regulatory approvals. Enrollment delays in our clinical trials may also result in increased development costs for our drug candidates, which could cause the value of our company to decline and limit our ability to obtain additional financing.

If serious adverse or unacceptable side effects are identified or we observe limited efficacy of our drugs or drug candidates, we may need to abandon or limit the development or commercialization of one or more of our drugs or drug candidates, and such findings may delay or prevent regulatory approval, limit commercial viability, or result in significant negative consequences following any marketing approval.

Four of our drug candidates are in clinical development for the treatment of human diseases. Their risk of failure is high. If our current or future indications of XPOVIO or any of our drug candidates 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 their development or limit development or 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, or AEs, in our clinical trials 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 XPOVIO were gastrointestinal, such as nausea, anorexia, diarrhea, vomiting, cytopenias, hyponatremia, constitutional symptoms of anorexia/weight loss, fatigue and neurological adverse reactions, including 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 were Grade 3 or Grade 4, meaning they were more than mild or moderate in severity, included thrombocytopenia, or low count of platelets in the blood, and neutropenia, or low neutrophil counts. 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. For example, among the 202 patients enrolled in Parts 1 and 2 of the STORM study who were treated with selinexor in combination with dexamethasone, the most common AEs (incidence $\geq 20\%$) were thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea, and upper respiratory tract infections. The treatment discontinuation rate in the STORM study due to AEs was 27%; 53% of patients had a reduction in the selinexor dose, and 65.3% had the dose of selinexor interrupted. In this group of patients, the most frequent AEs requiring permanent discontinuation in 4% or greater of patients who received selinexor included fatigue, nausea, and thrombocytopenia. Similarly, in the SADAL study, among the 134 patients included in the safety analysis, the most common AEs (incidence $\geq 20\%$) in patients with DLBCL were fatigue, nausea, diarrhea, appetite decrease, weight decrease, constipation, vomiting, and pyrexia. Grade 3-4 laboratory abnormalities ($\geq 15\%$) were thrombocytopenia, lymphopenia, neutropenia, anemia, and hyponatremia. The treatment discontinuation rate in the SADAL study due to AEs was 17%; 49% of patients had a reduction in the selinexor dose, and 61% had the dose of selinexor interrupted. Some patients across our clinical trials have experienced serious adverse events, or SAEs, deemed by us and the clinical investigator to be related to selinexor. SAEs 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 drug candidates approved for marketing or could result in the delay or denial of approval to market any drug candidates by the FDA or comparable foreign regulatory authorities, which could prevent us from generating sufficient revenue from the sale of drugs or achieving profitability. 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 and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our drug 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 drug 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;
- regulatory authorities may require additional warnings on the label or impose distribution or use restrictions;
- regulatory authorities may require one or more post-marketing studies;
- 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.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected drug candidate, if approved, or could substantially increase commercialization costs and expenses, which could delay or prevent us from generating sufficient revenue from the sale of our drugs and harm our business and results of operations.

The FDA or non-U.S. regulatory authorities may disagree with our and/or our clinical trial investigators' interpretation of data from clinical trials in determining if serious adverse or unacceptable side effects are drug-related.

We, and our clinical trial investigators, currently determine if serious adverse or unacceptable side effects are drug-related. The FDA or non-U.S. regulatory authorities may disagree with our or our clinical trial investigators' interpretation of data from clinical trials and the conclusion by us or our clinical trial investigators that a serious adverse effect or unacceptable side effect was not drug-related. The FDA or non-U.S. regulatory authorities may require more information, 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 drug candidates, and/or delay or cause us to change our commercialization plans, or we may decide to abandon the development or commercialization of the drug candidate altogether.

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

Because we have limited financial and managerial resources, we focus on research programs and drug candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other drug candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future research and development programs and drug candidates for specific indications may not yield any additional commercially-viable drugs. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug 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 drug candidate.

XPOVIO or any of our drug candidates that receive marketing approval may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

XPOVIO or any of our drug candidates that receive marketing approval may fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Efforts to educate the medical community and third-party payors on the benefits of our drug candidates require significant resources and may not be successful. For example, current cancer treatments like chemotherapy and radiation therapy are well-established in the medical community, and doctors may continue to rely on these treatments. If XPOVIO or our drug candidates do not achieve an adequate level of acceptance, we may not generate significant revenues from sales of drugs and we may not become profitable. The degree of market acceptance of XPOVIO for each approved indication and for our drug candidates, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- the ability to offer our drugs for sale at competitive prices;

- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- sufficient third-party coverage or reimbursement;
- effectiveness of our sales and marketing efforts;
- adverse publicity about our drugs or favorable publicity about competitive products;
- the prevalence and severity of any side effects;
- any restrictions on the use of our drugs together with other medications; and
- the inability of certain types of patients to take our drugs.

Our estimates of the potential market opportunities for XPOVIO and our drug 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, selinexor or any other drug 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.

If we are unable to maintain or expand our sales, marketing and distribution capabilities or maintain current agreements or enter into additional sales, marketing and distribution agreements with third parties, we may not be successful in commercializing XPOVIO or any of our drug candidates that we may develop if and when they are approved.

We have built a sales and marketing infrastructure 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 other drug candidates is approved for additional indications beyond hematological malignancies, we will need to substantially evolve our sales, marketing and distribution capabilities and we may not be able to do so successfully. In the future, we may choose to expand our sales, marketing and distribution infrastructure to market or co-promote one or more of our drug candidates, if and when they are approved, or enter into additional collaborations with respect to the sale, marketing and distribution of our drug candidates. We intend to work with existing and potential partners to establish the commercial infrastructure to support a potential launch of selinexor outside of the U.S.

There are risks involved with both establishing and maintaining our own sales, marketing and distribution capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time-consuming and could delay any commercial launch of a drug candidate. 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 drug candidates for which we establish a commercial infrastructure is delayed or does not occur for any reason, including if we do not receive marketing approval in the timeframe we expect, we would have prematurely or unnecessarily incurred these 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 commercialize XPOVIO or any drug candidates for which we receive marketing approval on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe current or future drugs;
- the lack of complementary drugs to be offered by sales personnel, 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
- existing or new competitors taking share from XPOVIO or preventing XPOVIO from gaining share in its approved indications.

Entering into arrangements with third parties to perform sales and marketing services may result in lower revenues from the sale of drug or the profitability of these revenues to us than if we were to market and sell any drugs that we develop ourselves. In addition, we may not be successful in maintaining current arrangements or entering into additional arrangements with third parties to sell, market and distribute XPOVIO or any of our drug candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our drugs effectively. Furthermore, we may be unable to enter into an arrangement with a third party if the current restrictions relating to COVID-19 continue to restrict travel, limit the ability of us or potential partners to negotiate and consummate a transaction in a timely manner, or if the COVID-19 pandemic causes a prolonged economic downturn. The extent to which the pandemic impacts our search for a partner will depend on future developments, which are highly uncertain and cannot be predicted, including additional information which may emerge concerning the severity of COVID-19 and the actions to contain COVID-19 or treat its impact, among others. If the disruptions posed by the COVID-19 pandemic or other matters of global concern continue for an extensive period of time, our ability to consummate an arrangement may be materially adversely affected.

If we do not successfully establish and maintain sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing XPOVIO or any of our drug candidates for which we obtain marketing approval.

We have a limited number of contractual arrangements with specialty pharmacies and specialty distributors. The specialty pharmacies sell XPOVIO directly to patients. The specialty distributors 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. Also, we may need to enter into agreements with additional pharmacies or distributors, and there is no guarantee that we will be able to do so on 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.

We may not receive royalty or milestone revenue under our partnership agreements for several years, or at all.

Certain of our partnership agreements provide for payments on achievement of development, regulatory and/or commercialization milestones and for royalties on product sales. However, because drug development entails a high risk of failure, we may never realize any material portion of the milestone revenue provided in our partnership agreements and we do not expect to receive any royalty revenue for several years, if at all.

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 face competition with respect to XPOVIO and our drug candidates and will face competition with respect to any drug candidates that we may seek to discover and develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. 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 are developing our drug candidates. Potential competitors also include academic institutions and governmental agencies and public and private research institutions.

We are initially focused on developing our current drug candidates for the treatment of cancer. 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. We expect that any of our drug candidates that are approved will be priced at a significant premium over competitive generic drugs. This may make it difficult for us to achieve our business strategy of using our drug candidates in combination with existing therapies or replacing existing therapies with our drug candidates.

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

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical studies, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. 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.

Even if we are able to effectively commercialize XPOVIO or any drug candidate that we may develop, the drugs 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. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or drug licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a drug in a particular country, but then be subject to price regulations that delay our commercial launch of the drug, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the drug in that country. In the U.S., approval and reimbursement decisions are not linked directly, but there is increasing scrutiny from the Congress and regulatory authorities of the pricing of pharmaceutical products. Adverse pricing limitations may also hinder our ability to recoup our investment in one or more drug candidates, even if our drug candidates obtain marketing approval.

Our ability to effectively commercialize XPOVIO or any of our product candidates that we may develop successfully will depend, in part, on the extent to which reimbursement for these drugs and related treatments 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 by third-party payors.

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 drug candidate that we 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 drug candidate for which we obtain marketing approval. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize XPOVIO or any drug candidate for which we obtain marketing approval.

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 regulatory authorities outside of the U.S. 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 drugs and our overall financial condition.

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

We face an inherent risk of product liability exposure related to the testing of our drug candidates in human clinical trials. We face an even greater risk as we commercialize XPOVIO or any other drugs that we may develop. 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 drug candidates or drugs caused injuries, we will incur substantial liabilities or be required to limit commercialization of our drug candidates. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for XPOVIO and any other drugs that we may develop;
- 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 drugs that we may develop.

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 conduct outside of the U.S. may be adversely affected by international risks and uncertainties.

Although our operations are based in the U.S., we 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 are seeking and continue to plan to seek approvals to sell our products in foreign countries. Any business that we conduct outside of the U.S. will be subject to additional risks that may materially adversely affect our 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 inflation, volatility in currency exchange rates or political instability in particular foreign economies and markets, including as a result of the current economic situation stemming from the COVID-19 pandemic;
- 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 pandemics (including the COVID-19 pandemic), geo-political actions, including war and terrorism, 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, or FCPA.

Risks Related to Our Financial Position, Convertible Senior Notes, Revenue Interest Financing Agreement and Need for Additional Capital

We have incurred significant losses since inception. We expect to continue to incur losses in the future and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss was \$152.9 million for the nine months ended September 30, 2020. As of September 30, 2020, we had an accumulated deficit of \$1.0 billion. With the launch of our first FDA-approved product, XPOVIO, in July 2019, we have had limited revenues to date from product sales and have historically financed our operations principally through private placements of our preferred stock, proceeds from our initial public offering and follow-on offerings of common stock, issuance of convertible debt, proceeds from a revenue interest financing agreement and cash generated from our business development activities. We have and continue to devote substantially all of our efforts to research and development, including preclinical studies and clinical trials, pursuing regulatory approvals and engaging in activities to commercially support XPOVIO in its two FDA-approved indications. Other than the FDA's two accelerated approvals of XPOVIO, our lead drug, oral selinexor (for indications not yet approved), as well as eltanexor, verdinexor, and KPT-9274, are in clinical development. Although we expect to continue to generate revenue from sales of XPOVIO, there can be no assurance as to the amount or timing of any such revenue, and we expect to continue to incur significant expenses and operating losses. The net losses we incur may fluctuate significantly from quarter to quarter.

We anticipate that we will continue to incur substantial expenses as we continue to commercialize XPOVIO in the U.S. and potentially outside of the U.S. and engage in activities to prepare for the potential approval and commercialization of additional indications for selinexor as well as our other drug candidates.

We anticipate that our expenses will increase substantially if and as we:

- continue to commercialize XPOVIO in the U.S., including the commercial launch of the recently approved DLBCL indication, and seek regulatory approval for XPOVIO outside of the U.S.;
- continue to grow our sales, marketing and distribution infrastructure to support the commercialization of XPOVIO and any drug candidates for which we may obtain marketing approval, prior to or upon receiving marketing approval in the U.S. or outside of the U.S.;
- continue our research and preclinical and clinical development of our drug candidates;
- initiate additional clinical trials for our drug candidates;
- seek marketing approvals for any of our drug candidates that successfully complete clinical trials;
- maintain, expand and protect our intellectual property portfolio;
- manufacture XPOVIO and our drug candidates;
- hire additional clinical, quality control, scientific, commercial and management personnel;
- identify additional drug candidates;
- acquire or in-license other drugs and technologies;
- add operational, financial and management information systems and personnel, including personnel to support our drug development, any commercialization efforts and our other operations as a public company; and
- increase our product liability insurance coverage as we grow our commercialization efforts.

Our ability to become and remain profitable depends on our ability to commercialize a drug or drugs with significant market potential, either on our own or with a collaborator. While we began to generate revenue from the sales of XPOVIO in July 2019, 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. This will require us to be successful in a range of challenging activities, including:

- continued successful commercialization of XPOVIO, including by maintaining our sales force, marketing and distribution capabilities;
- achieving an adequate level of market acceptance and obtaining and maintaining coverage and adequate reimbursement from third-party payors for XPOVIO and any other drugs we commercialize;
- completing preclinical studies and clinical trials of our drug candidates;
- obtaining marketing approval for these drug candidates;

- manufacturing at commercial scale, marketing, selling and distributing XPOVIO or any drug candidates for which we may obtain marketing approval;
- maintaining regulatory and marketing approvals for XPOVIO and for any drug candidates for which we obtain marketing approval;
- establishing and managing any collaborations for the development, marketing and/or commercialization of our drug candidates;
- hiring and building a full commercial organization required for the marketing, selling and distribution for those drugs for which we obtain marketing approval;
- navigating the negative impacts resulting from the ongoing COVID-19 pandemic to the healthcare systems and the ability of our clinical trial sites to conduct current or future trials; and
- obtaining, maintaining and protecting our intellectual property rights.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Our expenses could increase if we are required by the FDA or other regulatory authorities to perform clinical trials and non-clinical studies in addition to those that have been conducted or are currently expected, or if there are any delays in the development of our drug candidates or the manufacture of any of our drug candidates.

XPOVIO is our only product that has been approved for sale and it has only been approved in the U.S. Our ability to become and remain profitable will depend, in part, on the timing and success of commercial sales of XPOVIO for its two currently approved indications, which were commercially launched in the U.S. in July 2019 and June 2020, respectively. However, the successful commercialization of XPOVIO in the U.S. is subject to many risks. We do not anticipate 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 succeed in these activities and 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 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.

The nature and length of our operating history may make it difficult for stockholders to evaluate the success of our business to date and to assess our future viability.

We were incorporated in 2008 and commenced operations in 2009. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our platform, identifying potential drug candidates, conducting preclinical studies and early-phase and later-phase clinical trials of our drug candidates and commercializing XPOVIO. To date, we have not generated significant revenue from the sale of XPOVIO. Consequently, any predictions stockholders make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a business with a short operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We need to continue to successfully transition from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition. As we continue to build our business, we expect our financial condition and operating results may fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, stockholders should not rely upon the results of any particular quarterly or annual periods as indications of future operating performance.

We will need substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate our research and drug development programs or commercialization efforts.

We expect our expenses to increase in connection with our ongoing activities, particularly as we commercialize XPOVIO, including in the recently approved DLBCL indication, and continue the clinical trials of, and seek marketing approval and prepare for commercialization of, selinexor in additional indications and our other drug candidates. Our expenses have increased as we continue to commercialize XPOVIO, including costs associated with our sales force and increased marketing and distribution capabilities. If we obtain marketing approval for any drug candidates that we develop, we expect to incur significant additional commercialization expenses for such drug candidate to the extent that such sales, marketing, manufacturing and distribution functions are not the responsibility of any collaborator that we may have at such time for any such drug candidate. Furthermore, we will continue to incur additional costs associated with operating as a public company, hiring additional personnel and expanding our facilities. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. Further, any sustained disruption in the capital markets from the COVID-19 pandemic could negatively impact our ability to raise capital and we cannot predict the extent or duration of the macro-economic disruption stemming from the COVID-19 pandemic. If the macro-economic disruption continues for pro-longed periods, we may need to raise additional capital and capital may not be available on acceptable terms, or at all.

If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and drug development programs or any current or future commercialization efforts.

We expect 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. Our future capital requirements will depend on many factors, including:

- our ability to successfully commercialize XPOVIO in the U.S.;
- the cost of, and our ability to expand and maintain, the commercial infrastructure required to support the commercialization of XPOVIO and any other drug for which we receive marketing approval, including product sales, medical affairs, marketing and distribution;
- the progress and results of our current and planned clinical trials of selinexor;
- the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our other drug candidates;
- the costs, timing and outcome of regulatory review of our drug candidates, including whether any additional clinical trials or other activities are required for approval or label expansion;
- our ability to establish and maintain collaborations on favorable terms;
- the success of any collaborations that we have entered into and may enter into with third parties;
- the extent to which we acquire or in-license other drugs and technologies;
- the costs of commercialization activities, including costs related to product sales, marketing, manufacturing and distribution functions, for XPOVIO or any of our drug candidates for which we receive marketing approval, and pre-commercialization costs for our drug candidates incurred prior to receiving any such marketing approval, including the costs and timing of establishing product sales, marketing, manufacturing and distribution capabilities that are not the responsibility of any collaborator that we may have at such time;
- the amount of revenue, if any, received from commercial sales of our drug candidates, if approved;
- the terms and timing of any future collaborations, partnerships, licensing, marketing, distribution or other arrangements that we may establish; 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.

Identifying potential drug candidates, conducting preclinical studies and clinical trials, seeking marketing approvals and commercializing products are time-consuming, expensive and uncertain processes that take years to complete. Although we commercially launched XPOVIO in its two approved indications in July 2019 and June 2020, respectively, we do not anticipate that our revenue from product sales of XPOVIO will be sufficient for us to become profitable for several years, if at all. In addition, we may never generate the necessary data or results required to obtain marketing approval of our drug candidates. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. In addition, 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. Adequate additional financing may not be available to us on acceptable terms, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate development activities for one or more of our drug candidates or delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize XPOVIO or our drug candidates for which we obtain marketing approval.

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. For example, the COVID-19 pandemic has resulted in businesses suspending or terminating global operations and travel, self-imposed or government-mandated quarantines, and an overall slowdown of economic activity in many areas. 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 from the COVID-19 pandemic. If the equity and credit markets continue to 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. 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 from the COVID-19 pandemic, which could directly affect our ability to attain our operating goals on schedule and on budget.

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 Convertible Senior Notes due 2025, or Notes.

We incurred \$172.5 million of indebtedness as a result of the sale of the Notes and \$75.0 million as a result of the initial closing pursuant to the Revenue Interest Financing Agreement, or Revenue Interest Agreement, that we entered into with HealthCare Royalty Partners III, L.P. and HealthCare Royalty Partners IV, L.P., or HCR, on September 14, 2019. We may also incur additional indebtedness to meet future financing needs. 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 will 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 Notes; and
- placing us at a possible competitive disadvantage with competitors that are less leveraged than us or have better access to capital.

Our business may not generate sufficient funds, and we may otherwise be unable to maintain sufficient cash reserves, to pay amounts due under our indebtedness, including the Notes, and our cash needs may increase in the future.

Servicing the Notes will require a significant amount of cash, and we may not have sufficient cash flow from our business to make payments on our indebtedness.

Our ability to pay the principal of or interest and additional interest, if any, on the Notes or to make cash payments in connection with any conversion of the Notes depends on our future performance, which is subject 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 Notes or other future indebtedness and make necessary capital expenditures. In addition, if the impact of the COVID-19 pandemic to our results of operations and business prospects is more severe and prolonged than we currently anticipate, our ability to repay the Notes could be impaired. If we are unable to generate such cash flow, 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 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 or engage in these activities on desirable terms, which could result in a default on our debt obligations, including the Notes.

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

Holders may require us to repurchase their Notes following a fundamental change at a cash repurchase price generally equal to the principal amount of the Notes to be repurchased, plus accrued and unpaid interest and additional interest, if any. In addition, upon conversion, 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. We may not have enough available cash or be able to obtain financing at the time we are required to repurchase the Notes, pay cash amounts due upon conversion or redemption of the Notes or refinance the Notes. In addition, our ability to repurchase the Notes, to pay cash upon conversion or redemption of the Notes or to refinance the Notes may be limited by law, regulatory authority or agreements governing any future indebtedness that we may incur. Our failure to repurchase notes at a time when the repurchase is required by the indenture governing the Notes or to pay cash upon conversion of the 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 Notes or to pay cash upon conversion of the Notes.

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

In the event the conditional conversion feature of the Notes is triggered, holders of Notes will be entitled to convert the 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 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 that may be settled in cash, such as the Notes, could have a material effect on our reported financial results.

In May 2008, the Financial Accounting Standards Board, or FASB, issued FASB Staff Position No. APB 14-1, Accounting for Convertible Debt Instruments That May Be Settled in Cash upon Conversion (Including Partial Cash Settlement), which has subsequently been codified as Accounting Standards Codification 470-20, Debt with Conversion and Other Options, or ASC 470-20. Under ASC 470-20, an entity must separately account for the liability and equity components of the convertible debt instruments (such as the Notes) that may be settled entirely or partially in cash upon conversion in a manner that reflects the issuer's economic interest cost. The effect of ASC 470-20 on the accounting for the Notes is that the equity component is required to be included in the additional paid-in capital section of stockholders' equity at the issuance date, and the value of the equity component would be treated as debt discount for purposes of accounting for the debt component of the Notes. As a result, we will be required to record a greater amount of non-cash interest expense as a result of the amortization of the discounted carrying value of the Notes to their face amount over the term of the Notes. We will report a larger net loss in our financial results because ASC 470-20 will require interest to include both the amortization of the value of the debt discount and the instrument's coupon interest rate, which could adversely affect our future financial results, the market price of our common stock and the trading price of the Notes.

In addition, under certain circumstances, convertible debt instruments (such as the Notes) that may be settled entirely or partly in cash are currently eligible to be accounted for utilizing the treasury stock method, the effect of which is that the shares issuable upon conversion of the Notes are not included in the calculation of diluted earnings per share except to the extent that the conversion value of the Notes exceeds their principal amount. Under the treasury stock method, for diluted earnings per share purposes, the transaction is accounted for as if the number of shares of common stock that would be necessary to settle such excess, if we elected to settle such excess in shares, are issued. We cannot be sure that the accounting standards in the future will continue to permit the use of the treasury stock method. If we are unable to use the treasury stock method in accounting for the shares issuable upon conversion of the Notes, then our diluted earnings per share would be adversely affected.

Furthermore, if any of the conditions to the convertibility of the Notes is satisfied, then we may be required under applicable accounting standards to reclassify the liability carrying value of the Notes as a current, rather than a long-term, liability. This reclassification could be required even if no holders convert their Notes and could materially reduce our reported working capital.

Our Revenue Interest Agreement with HCR contains various covenants and other provisions, which, if violated, could result in the acceleration of payments due under such agreement.

On September 14, 2019, we entered into the Revenue Interest Agreement with HCR. Pursuant to the 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 and limits on 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. In addition, the Revenue Interest Agreement 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, HCR may accelerate payments due under the Revenue Interest Agreement up to \$138.8 million, less the aggregate of all of the payments previously paid to HCR. Upon the occurrence of specified material adverse events or the material breach of specified representations and warranties, which will not be considered events of default, HCR may elect to terminate the Revenue Interest Agreement and require us to make payments necessary for HCR to receive \$75.0 million, less the aggregate of all of the payments made to date, plus a specified annual rate of return. In the event that we are unable to make such payment, then HCR may be able to foreclose on the collateral that was pledged to HCR, which consists of all of our present and future assets relating to XPOVIO. Any such foreclosure remedy would significantly and adversely affect us and could result in us losing our interest in such assets.

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

Until such time, if ever, as we can generate substantial revenues from the sale of drugs, 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. Debt financing, if available, 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 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 HCR.

If we raise 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 drug 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 drug candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to Our Dependence on Third Parties

We depend on third parties for certain aspects of the development, marketing and/or commercialization of XPOVIO or our drug candidates and plan to enter into additional collaborations. If those collaborations are not successful, we may not be able to capitalize on the market potential of XPOVIO or our drug candidates.

We intend to maintain our existing collaborations and will continue to seek additional third-party collaborators for certain aspects of the development, marketing and/or commercialization of our drug candidates within and outside of the U.S. For example, we are parties to a license arrangement with Antengene Therapeutics Limited and a distribution agreement with Promedico Ltd. and plan to continue to seek to enter into additional license and distribution relationships, for marketing and commercialization of selinexor for other geographies 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 SINE compounds for indications outside of oncology. Potential collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. 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 drug candidates. 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. In addition, the third-parties upon whom we rely to develop, market and commercialize XPOVIO and our drug candidates could be negatively impacted by the COVID-19 pandemic, including as a result of businesses suspending or terminating global operations and travel, self-imposed or government-mandated quarantines, and an overall slowdown of economic activity. If our third-party collaborators are so affected, our business prospects and results of operations could be severely adversely impacted.

Collaborations involving our drug products and 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 regulatory requirements;
- collaborators may not pursue development, marketing and/or commercialization of our drug 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 drug candidate, repeat or conduct new clinical trials or require a new formulation of a drug candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, drugs that compete directly or indirectly with our drugs or drug candidates if the collaborators believe that competitive drugs 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 drugs may not commit sufficient resources to the marketing and distribution of such drug or drugs;

- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of drug candidates, might lead to additional responsibilities for us with respect to drug 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;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our drugs or drug candidates or that result in costly litigation or arbitration that diverts management's attention and resources of our company;
- 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 drugs or drug candidates;
- 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 collaborators or acquirers.

Collaboration agreements may not lead to development or commercialization of drug candidates in the most efficient manner, or at all. If our collaborations do not result in the successful development and commercialization of products or if 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, our development of our product candidates could be delayed and we may need additional resources to develop product candidates. 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 of our collaborators.

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 and specialty distributors to sell and distribute XPOVIO. 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 and lower product revenue, which would harm our results of operations and business.

If we are not able to maintain our existing collaborations or establish additional collaborations as we currently plan, we may have to alter our development and commercialization plans and our business could be adversely affected.

Our drug development programs and the commercialization of our drug candidates for which we receive marketing approval will require substantial additional cash to fund expenses. As noted above, we expect to maintain our existing collaborations and collaborate with additional pharmaceutical and biotechnology companies for the development of our drug candidates and the commercialization of our drugs or the potential commercialization of our drug candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, 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 similar regulatory authorities outside of the U.S., the potential market for the subject drug candidate, the costs and complexities of manufacturing and delivering such drug candidate to patients, the potential of competing drugs, 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. The collaborator may also consider alternative drug 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 for our drug candidate.

We may also be restricted under then-existing collaboration agreements from entering into future agreements on certain terms with potential collaborators.

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of such drug candidate, reduce or delay its development program or one or more of our other development programs, delay the commercialization of a drug or a drug candidate or reduce the scope of any sales or marketing activities, 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 drug candidates or bring them to market and generate revenue from sales of drugs.

We rely on some 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 some third parties, such as contract research organizations, 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 will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will 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 standards, commonly referred to as Good Clinical Practices, for conducting, recording and reporting the results of clinical trials to assure 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. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. 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, 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 drug candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our drug candidates. In such an event, our financial results and the commercial prospects for our drug candidates 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 drug candidates or commercialization of our drugs, producing additional losses and depriving us of potential revenue from sales of drugs.

In addition, as discussed above, the third-parties upon whom we rely to conduct our clinical trials could be negatively impacted as a result of disruptions caused by the COVID-19 pandemic, including difficulties in initiating clinical sites or enrolling participants, diversion of healthcare resources away from clinical trials, travel or quarantine policies, and other factors. If these third parties are so affected, our business prospects and results of operations could be severely adversely impacted.

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

We rely on academic and private non-academic institutions to conduct and sponsor clinical trials relating to selinexor and our other drug candidates. We do not control the design or conduct of the investigator-sponsored trials, and it is possible that the FDA or non-U.S. 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 or execution of the trials or safety concerns or other trial results.

Such arrangements will provide us certain information rights with respect to the investigator-sponsored trials, including 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 further clinical development of our drug candidates. Further, if investigators or institutions breach their obligations with respect to the clinical development of our drug 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 non-U.S. regulatory authorities may disagree with the sufficiency of our right of reference to 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 non-U.S. 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 contract with third parties for the manufacture of our drug candidates for preclinical studies and clinical trials and expect to continue to do so in connection with the commercialization of XPOVIO and for clinical trials and commercialization of any drug candidates that we develop and commercialize. This reliance on third parties increases the risk that we will not have sufficient quantities of our drug candidates or drugs or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not have any manufacturing facilities or personnel. We do not currently have nor do we plan to build internal infrastructure or capability to manufacture XPOVIO or our drug candidates for use in the conduct of our clinical trials or for commercial supply. We currently rely, and expect to continue to rely, on third-party manufacturers for the manufacture of our drug candidates for preclinical studies and clinical trials. We have engaged third-party manufacturers for drug substance and drug product services.

We have engaged a third-party contract manufacturer for the commercial production of XPOVIO and intend to do the same for any drug candidate that is approved by any regulatory agency. Reliance on third-party manufacturers entails risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible failure of the third party to manufacture our drugs or drug candidates according to our schedule, or at all, including if the third-party manufacturer gives greater priority to the supply of other drugs over our drugs and drug 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;
- the possible misappropriation or disclosure by the third party or others of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

This process is difficult and time consuming and we may face competition for access to manufacturing facilities, as there are a limited number of contract manufacturers operating under current Good Manufacturing Practices, or cGMPs, that are capable of manufacturing our drug candidates. 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 drug candidates that are subsequently approved.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the U.S. Facilities used by our third-party manufacturers must be inspected by the FDA after we submit an NDA and before potential approval of the drug candidate. Similar regulations apply to manufacturers of our drug candidates for use or sale in foreign countries. We do not control the manufacturing process and are completely dependent on our third-party manufacturers for compliance with the applicable regulatory requirements for the manufacture of our drug candidates. If our manufacturers cannot successfully manufacture material that conforms to the strict regulatory requirements of the FDA and any applicable foreign regulatory authority, they will not be able to secure the applicable approval for their manufacturing facilities. If these facilities are not approved for commercial manufacture, we may need to find alternative manufacturing facilities, which could result in delays in obtaining approval for the applicable drug candidate as alternative qualified manufacturing facilities may not be available on a timely basis, or at all. In addition, our manufacturers are subject to ongoing periodic unannounced inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements. Failure by any of our manufacturers to comply with applicable cGMPs 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 drug candidates and have a material adverse impact on our business, financial condition and results of operations. Any drugs that we may develop may compete with other drug candidates and drugs for access to manufacturing facilities.

Any performance failure on the part of our existing or future manufacturers could delay clinical development, marketing approval or commercialization of our drugs or drug candidates. For example, as a result of the COVID-19 pandemic, our suppliers and contract manufacturers could be disrupted by worker absenteeism, quarantines, or other travel or health-related restrictions or could incur increased costs associated with ensuring the safety and health of their personnel. 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 drug candidates or drugs, we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of XPOVIO or any drug candidates that we develop may adversely affect our future profit margins and our ability to commercialize any drugs that receive marketing approval on a timely and competitive basis.

Risks Related to Regulatory Approval and Marketing of Our Products and Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials for our product candidates, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our drug candidates in a timely manner, or at all. As a result, we cannot predict when or if we or any of our collaborators will obtain marketing approval to commercialize a drug candidate.

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of drugs are subject to extensive regulation by the FDA and comparable foreign regulatory authorities, whose laws and regulations may differ from country to country. We are not permitted to market our drug candidates in the U.S. or in other countries until we or any of our collaborators receive approval of an NDA from the FDA or marketing approval from applicable regulatory authorities outside of the U.S. In July 2019 and June 2020, the FDA approved XPOVIO in the multiple myeloma indication and the DLBCL indication, respectively. Continued approval for these indications may be contingent upon verification and description of clinical benefit in one or more confirmatory trials. For example, the FDA has agreed that the randomized Phase 3 BOSTON study evaluating selinexor in combination with Velcade® (bortezomib) and low-dose dexamethasone and the XPORT-DLBCL-030 study could serve as the confirmatory trials for the multiple myeloma and DLBCL indications, respectively. The BOSTON and XPORT-DLBCL-030 studies are post-marketing requirements for continued marketing authorization under the FDA's Accelerated Approval program issued by the FDA in July 2019 and June 2020, respectively, for XPOVIO based on the results of the STORM study and SADAL study, respectively. If the FDA does not approve our supplemental New Drug Application, or sNDA, submission based on the data from the BOSTON study, we will suffer substantial harm, including potential loss of the accelerated approval for XPOVIO based on the results of the STORM and SADAL studies.

In addition, in January 2019, we submitted an MAA to the EMA with a request for conditional approval of selinexor as a treatment for patients with heavily pretreated multiple myeloma based on the results of the STORM study. During March 2019, the EMA had inspectors conduct a Good Clinical Practices, or GCP, inspection at our headquarters, which was also attended by the FDA, as well as inspections of two clinical sites that participated in Part 2 of the STORM study. While we did not receive any findings from the FDA, in May 2019, the EMA inspectors provided us a written inspection report seeking our responses to various questions and findings. We promptly addressed the questions and findings in the inspection report and submitted proposals to the EMA's Committee for Medicinal Products for Human Use, or CHMP. In September 2019, we received the Day 180 List of Outstanding Issues from CHMP, which identified two issues requiring resolution. First, CHMP requested that we reconfirm the IRC adjudicated response rate to justify a positive benefit-risk assessment and, second, CHMP requested that we address the findings from the GCP inspection and our corrective measures taken to justify that the clinical trial data are of sufficient quality to support a benefit-risk assessment. In January 2020, we were granted a three-month extension to respond to the CHMP's outstanding questions related to the application. In September 2020, we submitted our responses following an additional extension of time due to the impact of the COVID-19 pandemic. In October 2020, we received a further updated list of outstanding issues, or LOI, from CHMP summarizing the remaining topics for us to address and indicating that, as part of its assessment of the safety and efficacy of selinexor based on the STORM study, the CHMP intends to consult its Scientific Advisory Group for additional advice in the fourth quarter of 2020. The LOI indicates that the CHMP is continuing to assess the IRC's adjudicated responses from the STORM study and asks us to justify the positive benefit-risk in the intended indication, which CHMP has also requested that we update to be more closely aligned with the patient population evaluated in the STORM study. The LOI further requests that we demonstrate that selinexor provides an advantage over approved therapies in the relevant indication and that we provide a summary of top-line data from the BOSTON study and the context of such data for the current application. We are currently in the process of preparing responses to the LOI; however, the CHMP may not be satisfied by our responses, might disagree with our responses or might request additional information, which may delay an opinion from the CHMP or result in a negative opinion by the CHMP, and ultimately the EMA, for selinexor in this indication.

With the exception of our sNDA submission to the FDA requesting approval of selinexor to treat multiple myeloma after at least one prior line of therapy, we have not submitted any other application for, or received any marketing approval of, any of our drug candidates in the U.S. or in any other jurisdiction. We have limited experience in conducting and managing the clinical trials necessary to obtain marketing approvals, including FDA approval of an NDA. The process of obtaining marketing approvals, both in the U.S. and abroad, is a lengthy, expensive and uncertain process. 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 drug candidates involved. In addition, we may experience delays in the regulatory review process for our drug candidates as a result of the ongoing COVID-19 pandemic, such as the EMA review of our MAA for selinexor in multiple myeloma based on the results on the STORM study and any resulting impact to the timing of our expected submission of an MAA for selinexor in multiple myeloma supported by the results of the BOSTON study or any future MAA submission.

Further, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted drug application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical studies, clinical trials or other studies and testing. In addition, varying interpretations of the data obtained from preclinical studies and clinical trials could delay, limit or prevent marketing approval of a drug candidate. Any marketing approval we or any of our collaborators ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved drug not commercially viable.

Any delay in obtaining or failure to obtain required approvals could materially adversely affect our ability or that of any of our collaborators to generate revenue from the particular drug candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

Under the FDA's accelerated approval regulations, we must still comply with post-approval development and regulatory requirements to maintain our approval of XPOVIO and, if we fail to do so, the FDA could withdraw its approval of XPOVIO for either of the currently approved indications, which would lead to substantially lower revenues.

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. As a condition of the accelerated approval of XPOVIO for the multiple myeloma indication, we are required to (i) complete and submit a final report with full datasets from the BOSTON study following completion of the study, (ii) conduct a randomized Phase 2 clinical trial of selinexor plus dexamethasone with three doses of selinexor including the approved dose of 80 mg on days one and three of each week and two doses that are lower than the approved dose, in a similar patient population for which XPOVIO is indicated (which we plan to conduct outside of the U.S.), (iii) conduct a trial with selinexor in patients who have mild, moderate or severe hepatic impairment, and (iv) conduct a drug interaction trial with selinexor in patients to evaluate the effect of co-administration of a strong CYP3A4 inhibitor on the pharmacokinetics of selinexor. As a condition of the accelerated approval of XPOVIO for the DLBCL indication, we are required to (i) complete and submit a final report with full datasets from a randomized, double-blind, placebo-controlled Phase 3 trial that verifies and describes the clinical benefit of selinexor in patients with relapsed or refractory DLBCL and (ii) provide the interim and final analyses of a randomized Phase 2 clinical trial of selinexor to characterize the safety and efficacy of at least two different dosing regimens of selinexor monotherapy in patients with relapsed or refractory DLBCL after at least two prior lines of systemic therapy.

The FDA may withdraw approval of XPOVIO for either approved indication if, for example, a trial required to verify the predicted clinical benefit of XPOVIO fails to verify such benefit or does not demonstrate sufficient clinical benefit to justify the risks associated with the drug. The FDA may also withdraw approval if other evidence demonstrates that XPOVIO is not shown to be safe or effective under the conditions of use, we fail to conduct any required post approval trial of our product candidate with due diligence or we disseminate false or misleading promotional materials relating to our product candidate. Similar risks to those described above are also applicable to any application that we have submitted or may submit to the EMA to support conditional approval of selinexor to treat heavily pretreated multiple myeloma, relapsed/refractory DLBCL, or any other cancer indication.

There can be no assurance that the FDA or any similar regulatory authority will determine that any confirmatory trial we conduct as part of our post-marketing obligations, will confirm that the surrogate marker used for accelerated approval of XPOVIO showed an adequate correlation with clinical outcomes. If the FDA or any similar regulatory authority determines that our confirmatory trials fail to show such adequate correlation, we may not be able to maintain our previously granted marketing approvals of XPOVIO.

Our failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad, and any approval we are granted for our product candidates in the U.S. does not assure approval of product candidates in foreign jurisdictions.

In order to market and sell our drugs in the European Union and many other jurisdictions, we and our current or future collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside of the U.S. generally includes all of the risks associated with obtaining FDA approval. In addition, 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. We and our collaborators may not obtain approvals from regulatory authorities outside of the U.S. on a timely basis, if at all. 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. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Additionally, in June 2016, the electorate in the United Kingdom, or UK, voted in favor of leaving the European Union, commonly referred to as Brexit. Following protracted negotiations, the UK left the European Union on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable up to two years). Discussions between the UK and the European Union have so far mainly focused on finalizing withdrawal issues and transition agreements but have been extremely difficult to date. To date, only an outline of a trade agreement has been reached. Much remains open but the Prime Minister has indicated that the UK will not seek to extend the transitional period beyond the end of 2020. If no trade agreement has been reached before the end of the transitional period, there may be significant market and economic disruption.

Since the regulatory framework for pharmaceutical products in the UK covering quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the UK. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the UK and/or European Union for our product candidates, which could significantly and materially harm our business.

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

Under the Federal Food, Drug and Cosmetic Act, or 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. Prior to seeking such accelerated approval, we will continue to seek feedback from the FDA and otherwise evaluate our ability to seek and receive such accelerated approval.

There can be no assurance that the FDA will agree with our surrogate endpoints or intermediate clinical endpoints in any of our clinical trials, or that we will decide to pursue or submit any additional NDAs for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that, after feedback from FDA, we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. 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.

A failure to obtain 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.

A fast track designation or breakthrough therapy status by the FDA is not assured and, in any event, may not actually lead to a faster development or regulatory review or approval process and, moreover, would not assure FDA approval of our product candidates.

We may be eligible for fast track designation or breakthrough therapy status for product candidates that we develop. If a product is intended for the treatment of a serious or life-threatening disease or condition and the product demonstrates the potential to address unmet medical needs for this disease or condition, the product sponsor may apply for FDA fast track designation. Additionally, a product candidate may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. The FDA has broad discretion whether or not to grant these designations, so even if we believe a particular product candidate is eligible for such designation or status, the FDA could decide not to grant it. Moreover, even if we do receive such a designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures and there is no assurance that our product candidate will be approved by the FDA. For example, in connection with our NDA for XPOVIO, in March 2019, the FDA extended the Prescription Drug User Fee Act, or PDUFA, action date by three months following our submission of additional, existing clinical information as an amendment to the NDA, which resulted in a nine-month review cycle despite the fast track designation. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

Priority review designation by the FDA may not lead to a faster regulatory review or approval process and, in any event, does not assure FDA approval of our product candidate.

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 FDA's goal to review an application is six months, rather than the standard review period of ten months. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may not grant it. Moreover, a priority review designation does not necessarily mean a faster regulatory review process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. For example, in connection with our NDA for XPOVIO, in March 2019, the FDA extended the PDUFA action date by three months following our submission of additional, existing clinical information as an amendment to the NDA, which resulted in a nine-month review cycle. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or thereafter.

We may not be able to obtain orphan drug exclusivity for our product candidates.

Regulatory authorities in some jurisdictions, including the U.S. and Europe, may designate drugs and biologics for relatively small patient populations as orphan drugs. 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, which is generally defined as a patient population of fewer than 200,000 individuals annually in the U.S.

Generally, if a product 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 EMA or the FDA from approving another marketing application for the same product for that time period. The applicable period is seven years in the U.S. and ten years in Europe. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may 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 patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity from the FDA for a product, as we have for XPOVIO as a treatment for patients with heavily pretreated multiple myeloma and selinexor in acute myeloid leukemia and DLBCL, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve a different product for the same condition if the FDA concludes 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.

On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017, or FDARA. 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. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Even if we or any of our collaborators obtain marketing approvals for our drug candidates, the terms of approvals and ongoing regulation of our drugs may limit how we, or they, manufacture and market our drugs, which could materially impair our ability to generate revenue.

Once marketing approval has been granted, an approved drug and its manufacturer and marketer are subject to ongoing review and extensive regulation. We and our collaborators must therefore comply with requirements concerning advertising and promotion for XPOVIO or for any of our drug candidates for which we or they obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the drug's approved labeling. Thus, we and our collaborators may not be able to promote any drugs we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved drugs and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, 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 to monitor and ensure compliance with cGMPs.

Accordingly, in connection with our currently approved products and assuming we or our current or future collaborators receive marketing approval for one or more of our drug 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, regulatory authorities could withdraw the marketing approvals of our drugs, and our or our collaborators' ability to market any future drugs 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.

XPOVIO and any of our drug candidates for which we or our collaborators obtain marketing approval in the future 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 drugs following approval.

XPOVIO and any of our drug 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 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, requirements regarding the distribution of samples to physicians and recordkeeping. For example, as a condition of the XPOVIO approval for the multiple myeloma and DLBCL indications, we are required to complete certain post-marketing commitments, as described above. Even if marketing approval of a drug 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 Risk Evaluation and Mitigation Strategy, which could include requirements for a restricted distribution system.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a drug. The FDA and other agencies, including the Department of Justice, or 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 do not market any of our drug candidates for which we, or they, receive marketing approval for only their approved indications, we, or they, may be subject to warnings or enforcement action for off-label marketing. Violation of the FDCA and other statutes, including the False Claims Act, 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. In addition, later discovery of previously unknown AEs or other problems with our drugs or their manufacturers or 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 such drugs, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a drug;
- restrictions on drug distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the drugs from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of drugs;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of drugs;
- drug seizure; or
- injunctions or the imposition of civil or criminal penalties.

Under the Cures Act and the Trump Administration's regulatory reform initiatives, the FDA's policies, regulations and guidance may be revised or revoked and that could prevent, limit or delay regulatory approval of our product candidates, which would impact our ability to generate revenue.

In December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and spur innovation. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the U.S. or abroad. For example, certain policies of the Trump Administration may impact our business and industry. Namely, the Trump Administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. An under-resourced FDA could result in delays in the FDA's responsiveness or in its ability to review submissions or applications, issue regulations or guidance, or implement or enforce regulatory requirements in a timely fashion, or at all. In January 2017, President Trump issued an executive order, applicable to all executive agencies including the FDA, which requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation and approximate the total costs or savings associated with each new regulation or repealed regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within the Office of Management and Budget in February 2017, the Trump Administration indicated that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. In addition, on February 24, 2017, President Trump issued an executive order directing each affected agency to designate an agency official as a "Regulatory Reform Officer" and establish a "Regulatory Reform Task Force" to implement the two-for-one provisions and other previously issued executive orders relating to the review of federal regulations. More recently, on October 9, 2019, President Trump issued another executive order ("Executive Order on Promoting the Rule of Law Through Improved Agency Guidance Documents"). The order is meant to ensure that agency guidance documents do not establish legally binding requirements and it directs each agency to rescind guidance documents that it determines should no longer be in effect.

In response to the COVID-19 pandemic, the Trump Administration is looking for additional ways to provide regulatory relief. It is difficult to predict how these various requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

With the recent 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 drug products on commercially reasonable, market-based terms for testing in support of their ANDAs and 505(b)(2) applications.

On December 20, 2019, 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, or 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 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) applicant must take certain steps to request the reference product, which, in the case of products covered by a risk evaluation and mitigation strategy with elements to assure safe use, include obtaining authorization from the FDA for the acquisition of the reference product. If the applicant 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 applicant 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 new 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 drug 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 other drug candidates, if approved, which could impact our ability to maximize product revenue.

Current and future legislation may increase the difficulty and cost for us and any collaborators to obtain marketing approval and commercialize our drug candidates 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 drug 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 drug 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 drugs.

Among the provisions of the Patient Protection and Affordable Care Act, or ACA, of potential importance to our business, including, without limitation, our ability to commercialize our drugs and the prices we may obtain for any of our drug candidates that are approved for sale, are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;

- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer point-of-sale discounts off negotiated prices to eligible beneficiaries during their coverage gap period, as a condition for a manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in April 2013 and, due to subsequent legislative amendments, will stay in effect through 2029 unless additional Congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. The CARES Act, which was signed into law on March 27, 2020 and designed to provide financial support and resources to individuals and businesses affected by the COVID-19 pandemic, suspended the 2% Medicare sequester from May 1, 2020 to December 31, 2020 and extended the sequester by one year, through 2030, in order to offset the added expense of the 2020 cancellation. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for XPOVIO and for any of our product candidates for which we may obtain regulatory approval or the frequency with which XPOVIO or any product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

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, new payment methodologies and additional downward pressure on the price that we receive for XPOVIO or any other approved product and/or the level of reimbursement physicians receive for administering XPOVIO or any other approved product we 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.

Some of the provisions of the ACA have yet to be implemented, and there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump Administration to repeal or replace certain aspects of the ACA. Since January 2017, President Trump has signed two executive orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Congress has considered legislation that would repeal or replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017, or the TCJA, includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. The Bipartisan Budget Act of 2018, among other things, amended the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". In July 2018, the Centers for Medicare and Medicaid Services, or CMS, published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment.

In addition, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseparable feature of the ACA, and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. The Trump Administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. The Trump Administration recently represented to the Court of Appeals considering this judgment that it does not oppose the lower court's ruling. On July 10, 2019, the Court of Appeals for the Fifth Circuit heard oral argument in this case. On December 18,

2019, that court affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. On January 21, 2020, the U.S. Supreme Court declined to review this decision on an expedited basis, but, on March 3, 2020, the Court agreed to hear the case. Subsequently, on June 25, 2020, the Trump Administration and a coalition of 18 states asked the court to strike down the entirety of the ACA. Oral argument before the Supreme Court is scheduled for November 10, 2020. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. In January 2017, President Trump signed an executive order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second executive order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the ACA exchanges. At the same time, the Trump Administration announced that it will discontinue the payment of cost-sharing reduction, or CSR, payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain. Further, in July 2018 following a federal district court decision from New Mexico, the Trump Administration announced that it would be freezing payments to insurers under the ACA to cover sicker patients until it or Congress can address the appropriate methodology for calculating and making such payments. It remains to be seen how this action will affect the implementation of the ACA.

We will continue to evaluate the effect that the ACA and its possible repeal and replacement could have on our business. It is possible that repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. While the timing and scope of any potential future legislation to repeal and replace ACA provisions is uncertain in many respects, it is also possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with ACA coverage expansion provisions. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from XPOVIO or from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates.

Further, there have been several recent U.S. congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, the Trump Administration's budget proposal contains further drug price control measures that could be enacted during the budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Specifically, the Trump Administration's 2021 budget proposal includes a \$135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients and increase patient access to lower cost generic drugs and biosimilars. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump Administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

Specifically, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Trump Administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the Trump Administration issued a plan to lower drug prices. Under this blueprint for action, the Trump Administration indicated that the Department of Health and Human Services, or HHS, will take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies, advance biosimilars and generics to boost price competition, evaluate the inclusion of prices in drug makers' ads to enhance price competition, speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers, avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid, work to give Medicare Part D plan sponsors more negotiation power with drug makers, examine which Medicare Part B drug prices could be negotiated by Medicare Part D plans, improve the design of the Medicare Part B Competitive Acquisition Program, update Medicare's drug-pricing dashboard to increase transparency, prohibit Medicare Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance, and require that Medicare Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases.

On July 24, 2020, President Trump issued four executive orders that are intended to lower the costs of prescription drug products. The first order would require all federally qualified health centers to pass on to patients the discounts the health centers receive on insulin and epinephrine through Medicare's 340B Drug Discount Program. The second order would establish an international pricing index that would set the price Medicare Part B pays for the costliest medications covered under the program to the lowest price in other economically advanced countries. The third order is intended to reduce the costs of drugs by supporting the safe importation of prescription drugs. Specifically, the order calls upon the Department of Health and Human Services, or HHS, to facilitate grants to individuals of waivers of the prohibition of importation of prescription drugs that would allow patients to import FDA-approved drug products from abroad, so long as doing so would result in lower costs. In addition, the order would allow wholesalers and pharmacies to re-import both biological drugs and insulin that were originally manufactured in the U.S. and then exported for international sale. This action follows the publication of a proposed rulemaking on December 23, 2020, that, if finalized, would allow states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants would be required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. At the same time, the FDA issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products). Finally, the fourth order would end drug rebates used by health plan sponsors, pharmacies or pharmacy benefit managers, or PBMs, in operating the Medicare Part D program. Specifically, the order directs HHS to exclude from safe harbor protections under the federal anti-kickback statute retroactive price reductions that are not applied at the point-of-sale. Instead, the order requires HHS to establish new safe harbors that would allow health plan sponsors, pharmacies, and PBMs to pass on those discounts to consumers at point-of-sale in order to "lower the patient's out-of-pocket costs" and "permit the use of certain bona fide PBM service fees". Each of these orders directs the federal government to implement the initiatives outlined in the orders, meaning they will not have immediate effects. Finally, and more recently, President Trump issued a fifth order, which instructs the federal government to develop a list of "essential" medicines and then buy them and other medical supplies from U.S. manufacturers instead of from companies around the world, including especially China. The order is intended to reduce regulatory barriers to domestic pharmaceutical manufacturing and catalyze manufacturing technologies needed to keep drug prices low and the production of drug products in the U.S.

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 health care authorities 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 health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

Moreover, legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical drugs. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our drug candidates, if any, may be. In addition, increased scrutiny by the Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any collaborators to more stringent drug labeling and post-marketing testing and other requirements.

Our relationships with healthcare providers and physicians and third-party payors are 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 providers, physicians and third party payors play a primary role in the recommendation and prescription of any drugs for which we obtain marketing approval. Our arrangements with third party payors, healthcare providers and physicians 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 any drugs for which we obtain marketing approval. These include the following:

- **Anti-Kickback Statute** - 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, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- **False Claims Act** - the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at a minimum of \$11,665 and a maximum of \$23,331 per false claim;

- **HIPAA** - the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters, and, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms and technical safeguards, with respect to maintaining the privacy, security and transmission of individually identifiable health information;
- **Transparency Requirements** - federal laws require applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals; and
- **Analogous State and Foreign Laws** - analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, can apply to sales or marketing arrangements and claims involving healthcare items or services and are generally broad and are enforced by many different federal and state agencies as well as through private actions.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations 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, imprisonment, exclusion of drugs 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 healthcare providers or entities with whom we do business is 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.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the European Union. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of European Union Member States, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the 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.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the EU General Data Protection Regulation, or the GDPR, which took effect across all member states of the European Economic Area, or EEA, in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside of the European Union, including the U.S. and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the U.S. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater, and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that European Union member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with the GDPR's requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

Similar actions are either in place or under way in the U.S. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act, which went into effect on January 1, 2020, is creating similar risks and obligations as those created by GDPR, though the California Consumer Privacy Act does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data. 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 reputation and our business.

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

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 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 any international operations we may have in the future may preclude us from developing, manufacturing and selling certain drug candidates 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 for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the DOJ. The SEC is involved with enforcement of the books and records provisions of the FCPA.

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 are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

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 drug candidates outside of the U.S., which could limit our growth potential and increase our development costs. 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.

Governments outside of the U.S. tend to impose strict price controls, which may adversely affect our revenues from the sales of drugs, if any.

In some countries, including the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we or our existing and future collaborators may be required to conduct a clinical trial that compares the cost-effectiveness of our drug to other available therapies. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

Inadequate funding for the FDA, the SEC and other government agencies 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. 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 drugs 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 FDA, SEC and other government 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, in our operations as a public company, 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.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our drug 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 drug 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 drug 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 drug candidates and other discoveries that are important to our business. As of October 15, 2020, 79 patents were in force that relate to XPO1 inhibitors, including composition of matter patents for selinexor, verdinexor and eltanexor in the U.S., and their use in targeted therapeutics. In addition, 16 patents were in force that relate to our PAK4/NAMPT inhibitors, including two composition of matter patents for KPT-9274 in the U.S. and its use in targeted therapeutics. We cannot be certain that any other patents will issue with claims that cover any of our key drug candidates or other discoveries or drug candidates.

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 drug 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, or 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 discoveries and drug candidates. Given the amount of time required for the development, testing and regulatory review of new drug 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 drug 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 drug 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 drugs, drug 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 drug 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 drug 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 we do not successfully extend the term of patents covering our drug 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 drug candidates, one or more of our U.S. patents may be eligible for patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as 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 drug candidates in all jurisdictions where these drug candidates are approved.

If we are unable to obtain a patent term extension for a drug 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 drug 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 drugs, drug 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, contract research organizations, 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 October 15, 2020, we have trademark registrations in the U.S. for our name and logo, and a combination of the two, XPOVIO, and PORE for our online portal. We also have pending applications in the U.S. to register two additional drug names (currently refused), and KARYFORWARD and a KARYFORWARD logo for our financial aid and charitable services. Outside the U.S., XPOVIO is registered or pending in forty-five additional jurisdictions, and is registered in Katakana in Japan, Hangul in South Korea, and Chinese characters in Taiwan. 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 drug 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 drug 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 Employee Matters and Managing Growth

Our future success depends on our ability to retain our Chief Executive Officer, our President and Chief Scientific Officer and other key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on Michael Kauffman, M.D., Ph.D., our Chief Executive Officer, and Sharon Shacham, Ph.D., M.B.A., our President and Chief Scientific Officer, as well as the other principal members of our management and scientific teams. Although we have entered into formal employment agreements with Drs. Kauffman and Shacham, 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 strategy. 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.

Drs. Kauffman and Shacham are married to each other. The separation or divorce of the couple in the future could adversely affect our business.

Dr. Kauffman, our Chief Executive Officer and member of our board of directors, and Dr. Shacham, our President and Chief Scientific Officer, are married to each other. They are two of our executive officers and are a vital part of our operations. If they were to become separated or divorced or could otherwise not amicably work with each other, one or both of them may decide to cease his or her employment with us or it could negatively impact our working environment. Alternatively, their work performance may not be satisfactory if they become preoccupied with issues relating to their personal situation. In these cases, our business could be materially harmed.

We have expanded and expect to continue to expand our development, regulatory and sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We have experienced and expect to continue to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, clinical operations, regulatory affairs, sales, marketing and distribution. To manage our current and anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing such growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Our business and operations may be materially adversely affected in the event of computer 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 contract research organizations and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, cyber attacks, natural disasters, fire, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. 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 drug candidates could be delayed or halted. We may also be vulnerable to cyber attacks by hackers, or other malfeasance. This type of breach of our cybersecurity may compromise our confidential information and/or our financial information and adversely affect our business or result in legal proceedings. In addition, the cost and operational consequences of implementing further data protection measures could be significant. Moreover, because the techniques used to obtain unauthorized access, disable or degrade service or sabotage systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or to implement adequate security measures.

Risks Related to Our Common Stock

Our executive officers, directors and principal stockholders maintain the ability to control all matters submitted to stockholders for approval.

As of October 15, 2020, our executive officers, directors and a small number of stockholders own more than a majority of our outstanding common stock. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

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.

An active trading market for our common stock may not be sustained.

Although our common stock is listed on The Nasdaq Global Select Market, an active trading market for our shares may not be sustained. If an active market for our common stock does not continue, it may be difficult for you to sell shares of our common stock without depressing the market price for the shares, or at all. An inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

If securities analysts do not continue to publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

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. There can be no assurance that analysts will provide favorable coverage or continue to cover us. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. 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.

The price of our common stock has been and may be volatile in the future and fluctuate substantially.

Our stock price has been and is likely to be volatile and may fluctuate substantially. For example, since October 15, 2019, our common stock has traded at prices per share as high as \$29.61 and as low as \$10.12. On October 30, 2020, the closing sale price of our common stock on The Nasdaq Global Select Market was \$14.82 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 recent response to the ongoing COVID-19 pandemic and related world-wide economic disruptions. The market price for our common stock may be influenced by many factors, including:

- our success in commercializing XPOVIO;
- the success of competitive drugs or technologies;
- results of clinical trials of our drug candidates or those of our competitors;
- our success in commercializing our drug candidates, if and when approved;
- regulatory or legal developments in the U.S. and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to the commercialization of XPOVIO and clinical development programs for any of our drug candidates;
- the results of our efforts to discover, develop, acquire or in-license additional drug candidates or drugs;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;

- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors, including as the result of uncertainties due to the ongoing COVID-19 pandemic;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

Securities litigation or other litigation could result in substantial damages and may divert management’s time and attention from our business.

In the past, securities class action litigation has often been brought against a company following a decline 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. We are a target of this type of litigation. See Part II, Item 1, “Legal Proceedings” in this Quarterly Report on Form 10-Q for information concerning securities litigation recently initiated against us and certain of our executive officers and directors and certain other defendants. We may become the target of additional securities litigation in the future. For example, we may face additional securities class action litigation or other litigation 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 drug 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 and cash equivalents and may not use them effectively.

Our management has broad discretion to use our cash and cash equivalents 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 drug 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.

We have incurred and will continue to incur increased costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives and corporate governance practices.

As a public company, we incur significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the SEC and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time-consuming and costly especially since we are no longer an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, and are no longer able to take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are “emerging growth companies” and that were applicable to us prior to January 1, 2019.

Section 404 of the Sarbanes-Oxley Act of 2002 requires us, on an annual basis, to review and evaluate our internal controls. To maintain compliance with Section 404, we are required to document and evaluate our internal control over financial reporting, which has been both costly and challenging. We will need to continue to dedicate internal resources, continue to engage outside consultants and follow a detailed work plan to continue to assess and document the adequacy of internal control over financial reporting, continue to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. There is a risk that in the future neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

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, or 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, or 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 shareholders 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.

Recent changes in tax law may adversely affect our business or financial condition. The TCJA significantly revises the Internal Revenue Code of 1986, as amended. 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%, limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits.

As part of Congress’ response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, was enacted on March 18, 2020, and the CARES Act was enacted on March 27, 2020. Both contain numerous tax provisions. In particular, the CARES Act retroactively and temporarily (for taxable years beginning before January 1, 2021) suspends application of the 80%-of-income limitation on the use of net operating losses, which was enacted as part of the TCJA. It also provides that net operating losses arising in any taxable year beginning after December 31, 2017, and before January 1, 2021 are generally eligible to be carried back up to five years. The CARES Act also temporarily (for taxable years beginning in 2019 or 2020) relaxes the limitation of the tax deductibility for net interest expense by increasing the limitation from 30% to 50% of adjusted taxable income.

Regulatory guidance under the TCJA, the FFCR Act and the CARES Act is and continues to be forthcoming, and such guidance could ultimately increase or lessen their impact on our business and financial condition. It is also likely that Congress will enact additional legislation in connection with the COVID-19 pandemic, some of which could have an impact on us. In addition, it is uncertain if and to what extent various states will conform to the TCJA, the FFCR Act or the CARES Act.

Item 6. Exhibits.

Exhibit Number	Description of Exhibit
10.1*	Fifth Amendment to Lease, dated as of August 13, 2020, by and between the Registrant and AG-JCM Wells Avenue Property Owner, LLC.
10.2	Amended and Restated Letter Agreement, dated as of August 31, 2020, between the Registrant and Michael Kauffman, M.D., Ph.D. (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-36167) filed with the Commission on August 31, 2020).
10.3	Amended and Restated Letter Agreement, dated as of August 31, 2020, between the Registrant and Sharon Shacham, Ph.D., M.B.A. (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-36167) filed with the Commission on August 31, 2020).
10.4	Amended and Restated Letter Agreement, dated as of August 31, 2020, between the Registrant and Christopher B. Primiano (incorporated by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K (File No. 001-36167) filed with the Commission on August 31, 2020).
10.5	Letter Agreement, dated as of August 31, 2020, between the Registrant and Michael Mason (incorporated by reference to Exhibit 10.4 to the Registrant's Current Report on Form 8-K (File No. 001-36167) filed with the Commission on August 31, 2020).
10.6	Transition Agreement, dated as of September 25, 2020, between the Registrant and Christopher B. Primiano (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-36167) filed with the Commission on September 25, 2020).
10.7	Consulting Agreement, dated as of September 25, 2020, between the Registrant and Christopher B. Primiano (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-36167) filed with the Commission on September 25, 2020).
10.8*	Letter Agreement, dated as of October 1, 2020, between the Registrant and Ran Frenkel.
10.9*	Form of Incentive Stock Option Agreement under 2013 Stock Incentive Plan adopted August 25, 2020.
10.10*	Form of Nonstatutory Stock Option Agreement under 2013 Stock Incentive Plan adopted August 25, 2020.
10.11*	Form of Restricted Stock Unit Agreement under 2013 Stock Incentive Plan adopted August 25, 2020.
10.12*	Form of Nonstatutory Stock Option Agreement for Inducement Grants adopted August 25, 2020.
10.13*	2020 Israeli Equity Incentive Sub Plan to the 2013 Stock Incentive Plan.
10.14*	Form of Option Agreement under 2020 Israeli Equity Incentive Sub Plan to the 2013 Stock Incentive Plan.
10.15*	Form of Restricted Stock Unit Agreement under 2020 Israeli Equity Incentive Sub Plan to the 2013 Stock Incentive Plan.
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)

* Filed herewith.

** Furnished herewith.

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: November 2, 2020

By: _____
/s/ MICHAEL KAUFFMAN
Michael Kauffman, M.D., Ph.D.
Chief Executive Officer
(Principal executive officer)

Date: November 2, 2020

By: _____
/s/ MICHAEL MASON
Michael Mason
Senior Vice President, Chief Financial Officer and Treasurer
(Principal financial and accounting officer)

FIFTH AMENDMENT TO LEASE

This FIFTH AMENDMENT TO LEASE (this "Amendment") is dated as of August 13, 2020 (the "Effective Date") and is hereby entered into by and between AG- JCM Wells Avenue Property Owner, LLC ("Landlord"), a Delaware limited liability company, with an address of c/o Jumbo Capital Management, LLC, 1900 Crown Colony Drive, 4th Floor, Quincy, Massachusetts 02169, and Karyopharm Therapeutics Inc. ("Tenant"), a Delaware corporation, with an address of 85 Wells Avenue, 2nd Floor, Newton, Massachusetts 02459.

RECITALS

WHEREAS, Landlord, as successor-in-interest to NS Wells Acquisition LLC, and Tenant are parties to that certain Office Lease Agreement dated March 27, 2014 (the "Original Lease"), as amended by that First Amendment to Lease dated December 31, 2014 (the "First Amendment"), as amended by that Second Amendment to Lease dated October 22, 2015 (the "Second Amendment"), as amended by that Third Amendment to Lease dated February 28, 2018 (the "Third Amendment"), and as amended by that Fourth Amendment to Lease dated June 6, 2018 (the "Fourth Amendment"), and together with the Original Lease, the First Amendment, the Second Amendment and the Third Amendment, the "Lease", pursuant to which Landlord leases to Tenant approximately 98,502 rentable square feet of office space being comprised of (i) 29,933 rentable square feet on the second (2nd) floor (the "Second Amendment Premises"), (ii) 8,468 rentable square feet located on the third (3rd) floor (the "Expansion Premises A"), (iii) 7,766 rentable square feet located on the third (3rd) floor (the "Expansion Premises B"), (iv) 15,976 rentable square feet located on the third (3rd) floor (the "New Expansion Premises"), and (v) 36,359 rentable square feet located on the second (2nd) floor (the "Fourth Amendment Expansion Premises"), and together with the Second Amendment Premises, the Expansion Premises A, the Expansion Premises B, and the New Expansion Premises, the "Premises", located in the building located at 75-95 Wells Avenue, Newton, Massachusetts 02459 (the "Building");

WHEREAS, Landlord is in the process of installing electric vehicle charging infrastructure in the location shown on Exhibit A attached hereto and incorporated herein by reference (the "Charging Stations Area");

WHEREAS, Tenant has requested that Landlord permit Tenant to use two (2) spaces ("Tenant's EV Spaces") in the Charging Stations Area with dedicated electric vehicle charging stations for the two (2) spaces ("Charging Stations") solely for the purposes of parking and charging Tenant's vehicles and the vehicles of Tenant's employees, officers, directors, contractors and invitees ("Sole Use"); and

WHEREAS, subject to Tenant's timely payment to Landlord of the Tenant's EV Spaces Fee (as hereinafter defined), Landlord hereby permits Tenant to use the Tenant's EV Spaces pursuant to all terms and conditions set forth herein.

AGREEMENT

NOW, THEREFORE, in consideration of the mutual covenants contained herein and for other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, Landlord and Tenant hereby agree, as of the Effective Date, as follows:

1. Incorporation of Recitals. The recitals set forth above are true and correct, incorporated herein and made a part of this Amendment as if set forth herein in full.
2. Incorporation of Exhibits. The exhibits attached hereto are incorporated herein and made a part of this Amendment as if set forth herein in full.
3. Capitalized Terms and Conflicts. All capitalized terms used in this Amendment that are not defined in this Amendment shall have the meanings ascribed to such terms in the Lease. In the event of any conflict between the terms of the Lease and the terms of this Amendment, the definitions set forth in this Amendment shall supersede and control.
4. Tenant's EV Spaces. Commencing on the date on which the electric vehicle charging infrastructure is installed and fully operational for the Sole Use (the "EV License Commencement Date") through the EV License Expiration Date (as hereinafter defined) (the "Tenant's EV Spaces Term"), Landlord hereby grants Tenant the right and license to use the Tenant's EV Spaces, but only for the Sole Use. Landlord and Tenant hereby agree that this Amendment is not intended to create a tenancy or leasehold interest and Tenant's rights to use the Tenant's EV Spaces on the terms and conditions set forth herein are merely a privilege and accommodation. Notwithstanding anything to the contrary contained in the Lease, Tenant's use of the Tenant's EV Spaces shall be included within, and shall not be separate and apart from, Tenant's parking rights as set forth in Section 15 of the Fourth Amendment. For the purposes of clarity, Tenant's use of the Tenant's EV Spaces shall be included within and shall be considered to be part of the three hundred fifteen (315) parking spaces that Tenant may use as currently set forth in Section 15 of the Fourth Amendment. Except as otherwise expressly provided herein, all terms and conditions of the Lease regarding Tenant's parking rights shall apply to the Tenant's EV Spaces, including, without limitation, Section 28 of the Lease.
5. EV License Expiration Date. The terms of this Amendment shall terminate and expire on the earlier of (i) September 30, 2025, (ii) the expiration or termination of the Lease, or (iii) Tenant's default under this Amendment.
6. Fees For Use. In consideration of Tenant's use of the Tenant's EV Spaces, Tenant shall pay to Landlord a fee equal to Four Hundred Fifty and 00/100 Dollars (\$450.00) per month (the "Tenant's EV Spaces Fee"), which amount shall be inclusive of all electricity charges and fees related to use of the Charging Stations with no additional electricity charges and fees. The Tenant's EV Spaces Fee shall be due and payable by Tenant to Landlord on the first (1st) day of each calendar month included in the Tenant's EV Spaces Term, and for any portion of the calendar month at the beginning or end of the Tenant's EV Spaces Term, at the proportionate rate payable for such portion. In the event either of the Charging Stations is not operational for seven (7) consecutive days or Tenant otherwise is unable to use the Tenant's EV Spaces for its Sole Use and such interruption was caused by (i) Landlord's negligence or willful

misconduct, then Tenant, as its sole remedy, shall be entitled to a proportionate abatement of the Tenant's EV Spaces Fee for the period commencing on the eighth (8th) consecutive day and ending on the date on which such condition is remedied; (ii) Tenant's negligence or willful misconduct, then Tenant shall not be entitled to a proportionate abatement of the Tenant's EV Spaces Fee and (iii) neither Landlord nor Tenant's negligence or willful misconduct, then Tenant shall be entitled to one half of a proportionate abatement of the Tenant's EV Spaces Fee for the period commencing on the eighth (8th) consecutive day and ending on the date on which such condition is remedied.

7. **Indemnification.** To the fullest extent permitted by law, Tenant shall defend, indemnify, and hold harmless Landlord its trustees, officers, employees and agents from any claim, losses, suits, judgment, damages, costs and expenses arising out of any injury, death or property damage occurring in, on or about the Charging Stations Area or Landlord's land arising as a result of the use of the Charging Stations Area and/or the Tenant's EV Spaces or Charging Stations by Tenant, its agents or employees, or any guest, patron, invitee or other person using the Charging Stations Area and/or the Tenant's EV Spaces or Charging Stations pursuant hereto except to the extent arising solely due to Landlord's negligence or willful misconduct. Tenant shall promptly pay to Landlord, upon demand, an amount equal to any costs and expenses incurred by Landlord in repairing the Tenant's EV Spaces, Charging Stations and/or Charging Stations Area, where such repair was made necessary by the acts or omissions or willful misconduct of Tenant, its agents or employees, or any guest, patron, invitee of Tenant or other person affiliated with Tenant using the Tenant's EV Spaces, Charging Stations and/or Charging Stations Area pursuant hereto.
8. **Signs.** Tenant may request that Landlord install signs ("**Signs**") in the Charging Stations Area identifying Tenant's right to use the Tenant's EV Spaces, subject to Landlord's prior written consent, which shall not be unreasonably withheld, conditioned or delayed. Any such Signs consented to by Landlord shall be placed in the Charging Stations Area by Landlord, at Landlord's sole cost and expense, shall be subject to any and all applicable municipal ordinances and laws, and shall be removed by Tenant at the expiration of the Tenant's EV Spaces Term. Landlord shall use commercially reasonable efforts to prevent other tenants, occupants or invitees of the Building from using Tenant's EV Spaces.
9. **Alterations and Additions.** Tenant shall not be permitted to make any alterations or improvements to the Tenant's EV Spaces, Charging Stations and/or Charging Stations Area without the prior written consent of Landlord.
10. **Repairs.** Landlord shall maintain the Charging Stations in good working order and condition at Landlord's sole cost and expense, except where such repair was made necessary by the acts or omissions or willful misconduct of Tenant, its agents or employees, or any guest, patron, invitee of Tenant or other person affiliated with Tenant using the Tenant's EV Spaces, Charging Stations and/or Charging Stations Area pursuant hereto.
11. **Remedies.** In the event of any breach by Tenant hereunder, if such breach is (i) the failure to pay amounts required to be paid hereunder, such failure shall constitute a "default" under this Amendment if Tenant fails to cure such nonpayment within five (5) days following notice from the Landlord, or (ii) if such breach is nonmonetary in nature, such breach shall constitute a "default" under this Amendment if Tenant fails to cure such breach within thirty (30) days

following notice from Landlord. In the event of such an uncured default, Landlord may at any time thereafter, in its sole and unfettered discretion, notwithstanding any and all other rights, remedies and recourses afforded Landlord, at any time, hereunder or at law or in equity, terminate Tenant's right to use the Tenant's EV Spaces by any lawful means, in which case this Amendment shall terminate and Tenant shall immediately cease Tenant's use of the Tenant's EV Spaces. Any and all past due amounts to be paid by Tenant to Landlord pursuant to the terms and conditions of this Amendment shall accrue interest at the rate set forth in Section 4 of the Lease, and shall be subject to any and all administration charges and fees in connection therewith.

12. Assignment. Except with respect to a transferee pursuant to a Permitted Transfer as defined in Section 11.04 of the Lease or to a transferee pursuant to a Transfer approved by Landlord under Section 11.01 of the Lease, Tenant may not assign or sublease any of the Tenant's EV Spaces, by operation of law or otherwise, nor permit the use of the Tenant's EV Spaces, Charging Stations or Charging Stations Area by anyone other than Tenant, or its authorized agents or employees. Tenant shall not offer the Tenant's EV Spaces for "use" or "license" to any other entity, the general public, or any other persons. Any such assignment, sublease or permit shall, at Landlord's option, be null, void and of no effect, or shall constitute a default under this Amendment.
13. Insurance. In addition to any such insurance required to be maintained by Tenant under the terms and conditions of the Lease, Tenant, at its sole cost and expense, shall obtain and maintain in full force and effect insurance in the amounts and coverages as specified below:
 - a. *Automobile Liability Insurance*. Automobile liability insurance policy with a minimum of not less than \$1,000,000 per accident. Coverage shall be applicable to all owned, hired, non-owned vehicles placed, parked or used by and under the control of Tenant or its employees, agents, affiliates and officers. This coverage shall be provided on an occurrence based form, and Landlord, shall be named as additional insureds.

The minimum limits of insurance coverage required of Tenant with respect to this Amendment shall in no event limit the liability of Tenant with respect to this Amendment. Tenant shall deliver to Landlord evidence of the coverage required hereunder on or before the EV License Commencement Date, and delivery of such evidence shall be a prerequisite to and condition of Tenant's right to use the Tenant's EV Spaces and Charging Stations. All insurance required above shall otherwise comply with and be subject to all terms and conditions of the Lease. Tenant's compliance with the provisions of this Section shall in no way relieve or decrease Tenant's indemnification obligations under this Amendment or the Lease, or any of Tenant's other obligations hereunder or under the Lease.

14. Brokers. Landlord and Tenant represent and warrant to the other that they have not made any agreement or taken any action which may cause any other party to become entitled to a commission as a result of the transactions contemplated by this Amendment. Furthermore, each party will indemnify and defend the other from any and all claims, actual or threatened, for compensation by any other such third person by reason of such party's breach of their representation or warranty contained in this Section.

15. Hazardous Materials. Tenant will not keep or have on the Charging Stations Area any article or thing of a dangerous, flammable, or explosive character that might unreasonably increase the danger of fire at the Charging Stations Area or Landlord's land or that might be considered hazardous by any reputable insurance company.
16. Tenant's Representations. Tenant hereby represents and warrants, to the best of Tenant's knowledge, to Landlord that as of the Effective Date: (a) all of Tenant's estate, right, title and interest in and to the Lease is free and clear of assignments, sublettings, liens and encumbrances; (b) the Lease is in full force and effect; (c) Tenant is presently in possession of the Premises and is paying Base Rent, operating expenses and any other charges or sums due under the Lease with respect to the Premises; (d) the Lease has not been modified, supplemented or amended in any way, except as may be set forth in this Amendment; (e) Tenant is not aware of any actionable defenses, claims or set-offs under the Lease against rents or charges due or to become due thereunder; and (f) that this Amendment has been duly authorized, executed and delivered by and on behalf of Tenant and constitutes the valid and binding agreement of Tenant in accordance with the terms hereof.
17. Governing Law. This Amendment shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts without regard to the principles thereof relating to conflicts of law.
18. Ratification of Lease. Except as amended and modified by this Amendment, all the terms, provisions, agreements, covenants and conditions of the Lease are hereby affirmed and ratified
19. Authority. Each of Landlord and Tenant represents to the other that the representing party has the power and authority to execute, deliver and perform, and by all necessary action has authorized the execution, delivery and performance of, all of its obligations under this Amendment.
20. Execution/Entire Agreement. This Amendment, together with the Lease as affected hereby, constitutes the entire agreement of the parties, and may not be amended except by written instrument signed by all parties. This Amendment shall have the effect of an agreement under seal and shall be binding upon and inure to the benefit of the parties hereto and their respective successors and assigns.
21. Counterparts. This Amendment may be executed in multiple counterparts, each of which shall be deemed an original and all of which together shall constitute one and the same document. Each party hereto may rely upon an "e-signature" such as DocuSign, or a pdf of a counterpart of this Amendment or detailed signature page therefrom that has been executed by any other party hereto, as if the same were the executed original thereof, and the other party shall be bound thereby.

[Signature page follows]

IN WITNESS WHEREOF, Landlord and Tenant have caused this Amendment to be executed as of the date set forth above.

LANDLORD:

AG-JCM WELLS AVENUE PROPERTY OWNER, LLC
a Delaware limited liability company

By: /s/Jay Hirsh
Name: Jay O. Hirsh
Title: Authorized Signatory

TENANT:

KARYOPHARM THERAPEUTICS INC.
a Delaware corporation

By: /s/Christopher B. Primiano
Name: Christopher B. Primiano
Title: EVP, Chief Business Officer

October 1, 2020

Ran Frankel

Dear Ran:

You and Karyopharm Therapeutics Inc. (the “Company”) are parties to a letter agreement dated June 7, 2015, as amended on October 4, 2016, related to your employment as the Chief Development Operations Officer of the Company (the “Letter Agreement”). This letter is to inform you that, effective August 28, 2020 the Compensation Committee of the Board of Directors of the Company approved certain enhanced severance benefits for you, as described below, in addition to the benefits you may be entitled to under the Letter Agreement. Except as specifically set forth below, the Letter Agreement remains in full force and effect, and no provisions thereof are amended except as set forth below. Capitalized terms used but not defined herein shall have the meaning set forth in the Letter Agreement.

The first paragraph of the “*Severance Compensation*” section of the Letter Agreement shall be replaced with the following:

Severance Compensation. If the Company (which, for the purposes of this paragraph, includes any successor entity) terminates the term of your employment without Cause, or you resign for Good Reason, then provided that you execute a release of any and all claims that you may have against the Company arising from your employment with the Company, reasonably satisfactory to the Company in form and substance, which release becomes effective within 60 days following your termination, the Company (i) will continue to pay you your base compensation at its then-current rate, in accordance with the Company’s then-current regular payroll procedures for employees, for twelve (12) months (subject to upward adjustment in the event that standardized severance terms are authorized for all employees of your level and such terms exceed the severance amount provided herein) beginning in the first payroll period following the effectiveness of the release; and (ii) 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”), will pay the monthly premium to continue such coverage for the lesser of the twelve (12) full calendar months immediately following the month in which the termination of your employment occurs and 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 your employment is terminated without Cause, or you resign for Good Reason, in either case within one year following the consummation of a Change in Control (as defined below), then, provided that you execute a release of any and all claims that you may have against the Company arising from your employment with the Company, reasonably satisfactory to the Company in form and substance, which release

Karyopharm Therapeutics Inc.
85 Wells Avenue
Newton, MA 02459
www.karyopharm.com

becomes effective within 60 days following your termination, the Company (or its successor entity) will (i) continue to pay you your base compensation at its then-current rate, in accordance with the Company's (or successor's) then-current regular payroll procedures for employees, for at least twelve (12) months beginning in the first payroll period following the effectiveness of the release; (ii) 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 this agreement and (iii) provided you elect to continue your and your eligible dependents' participation in the Company's medical and dental benefit plans pursuant to COBRA, pay the monthly premium to continue such coverage for the lesser of the twelve (12) full calendar months immediately following the month in which the termination of your employment occurs and the end of the calendar month in which you become eligible to receive group health plan coverage under another employee benefit plan.

For the avoidance of doubt, that nothing herein supersedes the Non Disclosure, Inventions Assignment, Non-Competition, and Non-Solicitation Agreement you previously executed with the Company, which remains in effect, unaltered, in all respects.

Thank you for your continued commitment to Karyopharm!

Sincerely,

/s/ Michael Kauffman

Michael Kauffman, M.D., Ph.D.

KARYOPHARM THERAPEUTICS INC.
INCENTIVE STOCK OPTION AGREEMENT

Karyopharm Therapeutics Inc. (the "Company") hereby grants the following stock option pursuant to its 2013 Stock Incentive Plan. The terms and conditions attached hereto are also a part hereof.

Notice of Grant

Name of optionee (the " <u>Participant</u> "):	
Date of this option grant:	
Number of shares of the Company's Common Stock subject to this option (" <u>Shares</u> "):	
Option exercise price per Share:	
Number, if any, of Shares that vest immediately on the grant date:	
Shares that are subject to vesting schedule:	
Vesting Start Date:	
Final Exercise Date:	

Vesting Schedule:

One Year from Vesting Start Date:	
Each Successive month thereafter:	
Four Years from Vesting Start Date:	
All vesting is dependent on the Participant remaining an Eligible Participant, as provided herein.	

This option satisfies in full all commitments that the Company has to the Participant with respect to the issuance of stock, stock options or other equity securities.

KARYOPHARM THERAPEUTICS INC.

By:
 Name of Officer: Michael Mason
 Title: Chief Financial Officer

KARYOPHARM THERAPEUTICS INC.

Incentive Stock Option Agreement
Incorporated Terms and Conditions

1. Grant of Option.

This agreement evidences the grant by the Company, on the grant date (the "Grant Date") set forth in the Notice of Grant that forms part of this agreement (the "Notice of Grant"), to the Participant, an employee of the Company, of an option to purchase, in whole or in part, on the terms provided herein and in the Company's 2013 Stock Incentive Plan (the "Plan"), the number of Shares set forth in the Notice of Grant of common stock, \$0.0001 par value per share, of the Company ("Common Stock") at the exercise price per Share set forth in the Notice of Grant. Unless earlier terminated, this option shall expire at 5:00 p.m., Eastern time, on the Final Exercise Date set forth in the Notice of Grant (the "Final Exercise Date").

It is intended that the option evidenced by this agreement shall be an incentive stock option as defined in Section 422 of the Internal Revenue Code of 1986, as amended, and any regulations promulgated thereunder (the "Code"). Except as otherwise indicated by the context, the term "Participant", as used in this option, shall be deemed to include any person who acquires the right to exercise this option validly under its terms.

2. Vesting Schedule.

This option will become exercisable ("vest") in accordance with the vesting schedule set forth on the cover page of this agreement (the "Vesting Schedule"). Any fractional shares resulting from the application of any percentages used in the Vesting Table shall be rounded down to the nearest whole number of shares of Common Stock (except for the last vesting tranche).

Notwithstanding the foregoing, to the extent that the Participant is a party to an employment agreement or other agreement with the Company that provides vesting terms that differ from the Vesting Schedule, the terms set forth in such employment agreement or other agreement shall prevail.

The right of exercise shall be cumulative so that to the extent the option is not exercised in any period to the maximum extent permissible it shall continue to be exercisable, in whole or in part, with respect to all Shares for which it is vested until the earlier of the Final Exercise Date or the termination of this option under Section 3 hereof or the Plan.

3. Exercise of Option.

(a) Form of Exercise. Each election to exercise this option shall be in writing, in the form of the Stock Option Exercise Notice attached as Annex A, signed by the Participant, and received by the Company at its principal office, accompanied by this agreement, or in such other form, which may be electronic, as determined by the Company, together with payment in full of

the exercise price and any applicable tax withholding in the manner provided in the Plan. The Participant may purchase less than the number of shares covered hereby, provided that no partial exercise of this option may be for any fractional share.

(b)Continuous Relationship with the Company Required. Except as otherwise provided in this Section 3, this option may not be exercised unless the Participant, at the time he or she exercises this option, is, and has been at all times since the Grant Date, an employee, director or officer of, or consultant or advisor to, the Company or any parent or subsidiary of the Company as defined in Section 424(e) or (f) of the Code (an “Eligible Participant”).

(c)Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (d) and (e) below, the right to exercise this option shall terminate three months after such cessation (but in no event after the Final Exercise Date), provided that this option shall be exercisable only to the extent that the Participant was entitled to exercise this option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the non-competition or confidentiality provisions of any employment contract, confidentiality and nondisclosure agreement or other agreement between the Participant and the Company, the right to exercise this option shall terminate immediately upon such violation.

(d)Exercise Period Upon Death or Disability. If the Participant dies or becomes disabled (within the meaning of Section 22(e)(3) of the Code) prior to the Final Exercise Date while he or she is an Eligible Participant and the Company has not terminated such relationship for “cause” as specified in paragraph (e) below, this option shall be exercisable, within one year following the date of death or disability of the Participant, by the Participant (or in the case of death by an authorized transferee), provided that this option shall be exercisable only to the extent that this option was exercisable by the Participant on the date of his or her death or disability, and further provided that this option shall not be exercisable after the Final Exercise Date.

(e)Termination for Cause. If, prior to the Final Exercise Date, the Participant’s employment is terminated by the Company for Cause (as defined below), the right to exercise this option shall terminate immediately upon the effective date of such termination of employment. “Cause” shall mean, in the good faith determination of the Company, the Participant has: (i) committed gross negligence or willful malfeasance in the performance of the Participant’s work or duties; (ii) committed a breach of fiduciary duty or a breach of any non-competition, non-solicitation or confidentiality obligations to the Company; (iii) failed to follow the proper directions of the Participant’s direct or indirect supervisor after written notice of such failure; (iv) been convicted of, or pleaded “guilty” or “no contest” to, any misdemeanor relating to the affairs of the Company or any felony; (v) disregarded the material rules or material policies of the Company which has not been cured within 15 days after notice thereof from the Company; or (vi) engaged in intentional acts that have generated material adverse publicity toward or about the Company.

4. Tax Matters.

(a) Withholding. No Shares will be issued pursuant to the exercise of this option unless and until the Participant pays to the Company, or makes provision satisfactory to the Company for payment of, any federal, state or local withholding taxes required by law to be withheld in respect of this option.

(b) Disqualifying Disposition. If the Participant disposes of Shares acquired upon exercise of this option within two years from the Grant Date or one year after such Shares were acquired pursuant to exercise of this option, the Participant shall notify the Company in writing of such disposition.

(c) Reporting. The Participant acknowledges and agrees to comply with all necessary reporting obligations in the Participant's jurisdiction in relation to all taxes, social security contributions and any other similar charges which arise in relation to this option.

5. Transfer Restrictions.

This option may not be sold, assigned, transferred, pledged or otherwise encumbered by the Participant, either voluntarily or by operation of law, except by will or the laws of descent and distribution, and, during the lifetime of the Participant, this option shall be exercisable only by the Participant.

6. Participant's Acknowledgement of Clawback.

The Participant acknowledges that in accepting this award, the Participant will be bound by any clawback policy that the Company has in place or may adopt in the future.

7. Provisions of the Plan.

This option is subject to the provisions of the Plan (including the provisions relating to amendments to the Plan), a copy of which is furnished to the Participant with this option.

KARYOPHARM THERAPEUTICS INC.

Stock Option Exercise Notice

Karyopharm Therapeutics Inc.
85 Wells Avenue
Newton, MA 02459

Dear Sir or Madam:

I, _____ (the "Participant"), hereby irrevocably exercise the right to purchase _____ shares of the Common Stock, \$.0001 par value per share (the "Shares"), of Karyopharm Therapeutics Inc. (the "Company") at \$ _____ per share pursuant to the Company's 2013 Stock Incentive Plan and a stock option agreement with the Company dated _____ (the "Option Agreement"). Enclosed herewith is a payment of \$ _____, the aggregate purchase price for the Shares. The certificate for the Shares should be registered in my name as it appears below or, if so indicated below, jointly in my name and the name of the person designated below, with right of survivorship.

Dated:

Signature

Print Name:

Address:

Name and address of persons in whose name the Shares are to be jointly registered (if applicable):

KARYOPHARM THERAPEUTICS INC.
NONSTATUTORY STOCK OPTION AGREEMENT

Karyopharm Therapeutics Inc. (the "Company") hereby grants the following stock option pursuant to its 2013 Stock Incentive Plan. The terms and conditions attached hereto are also a part hereof.

Notice of Grant

Name of optionee (the " <u>Participant</u> "):	
Date of this option grant:	
Number of shares of the Company's Common Stock subject to this option (" <u>Shares</u> "):	
Option exercise price per Share:	
Number, if any, of Shares that vest immediately on the grant date:	
Shares that are subject to vesting schedule:	
Vesting Start Date:	
Final Exercise Date:	

Vesting Schedule:

One Year from Vesting Start Date:	
Each Successive month thereafter:	
Four Years from Vesting Start Date:	
All vesting is dependent on the Participant remaining an Eligible Participant, as provided herein.	

This option satisfies in full all commitments that the Company has to the Participant with respect to the issuance of stock, stock options or other equity securities.

KARYOPHARM THERAPEUTICS INC.

Signature of Participant

By:
Name of Officer: Michael Mason
Title: Chief Financial Officer

Street Address

City/State/Zip Code

KARYOPHARM THERAPEUTICS INC.

Nonstatutory Stock Option Agreement
Incorporated Terms and Conditions

1. Grant of Option.

This agreement evidences the grant by the Company, on the grant date (the "Grant Date") set forth in the Notice of Grant that forms part of this agreement (the "Notice of Grant") to the Participant of an option to purchase, in whole or in part, on the terms provided herein and in the Company's 2013 Stock Incentive Plan (the "Plan"), the number of Shares set forth in the Notice of Grant of common stock, \$0.0001 par value per share, of the Company ("Common Stock") at the exercise price per Share set forth in the Notice of Grant. Unless earlier terminated, this option shall expire at 5:00 p.m., Eastern time, on the Final Exercise Date set forth in the Notice of Grant (the "Final Exercise Date").

It is intended that the option evidenced by this agreement shall not be an incentive stock option as defined in Section 422 of the Internal Revenue Code of 1986, as amended, and any regulations promulgated thereunder (the "Code"). Except as otherwise indicated by the context, the term "Participant", as used in this option, shall be deemed to include any person who acquires the right to exercise this option validly under its terms.

2. Vesting Schedule.

This option will become exercisable ("vest") in accordance with the vesting schedule set forth on the cover page of this agreement (the "Vesting Schedule"). Any fractional shares resulting from the application of any percentages used in the Vesting Table shall be rounded down to the nearest whole number of shares of Common Stock (except for the last vesting tranche).

Notwithstanding the foregoing, to the extent that the Participant is a party to an employment agreement or other agreement with the Company that provides vesting terms that differ from the Vesting Schedule, the terms set forth in such employment agreement or other agreement shall prevail.

The right of exercise shall be cumulative so that to the extent the option is not exercised in any period to the maximum extent permissible it shall continue to be exercisable, in whole or in part, with respect to all Shares for which it is vested until the earlier of the Final Exercise Date or the termination of this option under Section 3 hereof or the Plan.

3. Exercise of Option.

(a) Form of Exercise. Each election to exercise this option shall be in writing, in the form of the Stock Option Exercise Notice attached as Annex A, signed by the Participant, and received by the Company at its principal office, accompanied by this agreement, or in such other form, which may be electronic, as determined by the Company, together with payment in full of the exercise price and any applicable tax withholding in the manner provided in the Plan. The

Participant may purchase less than the number of shares covered hereby, provided that no partial exercise of this option may be for any fractional share.

(b)Continuous Relationship with the Company Required. Except as otherwise provided in this Section 3, this option may not be exercised unless the Participant, at the time he or she exercises this option, is, and has been at all times since the Grant Date, an employee, director or officer of, or consultant or advisor to, the Company or any other entity the employees, officers, directors, consultants, or advisors of which are eligible to receive option grants under the Plan (an “Eligible Participant”).

(c)Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (d) and (e) below, the right to exercise this option shall terminate three months after such cessation (but in no event after the Final Exercise Date), provided that this option shall be exercisable only to the extent that the Participant was entitled to exercise this option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the non-competition or confidentiality provisions of any employment contract, confidentiality and nondisclosure agreement or other agreement between the Participant and the Company, the right to exercise this option shall terminate immediately upon such violation.

(d)Exercise Period Upon Death or Disability. If the Participant dies or becomes disabled (within the meaning of Section 22(e)(3) of the Code) prior to the Final Exercise Date while he or she is an Eligible Participant and the Company has not terminated such relationship for “cause” as specified in paragraph (e) below, this option shall be exercisable, within one year following the date of death or disability of the Participant, by the Participant (or in the case of death by an authorized transferee), provided that this option shall be exercisable only to the extent that this option was exercisable by the Participant on the date of his or her death or disability, and further provided that this option shall not be exercisable after the Final Exercise Date.

(e) Termination for Cause. If, prior to the Final Exercise Date, the Participant’s employment or other relationship with the Company is terminated by the Company for Cause (as defined below), the right to exercise this option shall terminate immediately upon the effective date of such termination of employment or other relationship. “Cause” shall mean, in the good faith determination of the Company, the Participant has: (i) committed gross negligence or willful malfeasance in the performance of the Participant’s work or duties; (ii) committed a breach of fiduciary duty or a breach of any non-competition, non-solicitation or confidentiality obligations to the Company; (iii) failed to follow the proper directions of the Participant’s direct or indirect supervisor after written notice of such failure; (iv) been convicted of, or pleaded “guilty” or “no contest” to, any misdemeanor relating to the affairs of the Company or any felony; (v) disregarded the material rules or material policies of the Company which has not been cured within 15 days after notice thereof from the Company; or (vi) engaged in intentional acts that have generated material adverse publicity toward or about the Company.

4. Withholding.

No Shares will be issued pursuant to the exercise of this option unless and until the Participant pays to the Company, or makes provision satisfactory to the Company for payment of, any federal, state or local withholding taxes required by law to be withheld in respect of this option.

5. Reporting.

The Participant acknowledges and agrees to comply with all necessary reporting obligations in the Participant's jurisdiction in relation to all taxes, social security contributions and any other similar charges which arise in relation to this option.

6. Transfer Restrictions.

This option may not be sold, assigned, transferred, pledged or otherwise encumbered by the Participant, either voluntarily or by operation of law, except by will or the laws of descent and distribution, and, during the lifetime of the Participant, this option shall be exercisable only by the Participant.

7. Participant's Acknowledgement of Clawback. The Participant acknowledges that in accepting this award, the Participant will be bound by any clawback policy that the Company has in place or may adopt in the future.

8. Provisions of the Plan.

This option is subject to the provisions of the Plan (including the provisions relating to amendments to the Plan), a copy of which is furnished to the Participant with this option.

KARYOPHARM THERAPEUTICS INC.

Stock Option Exercise Notice

Karyopharm Therapeutics Inc.
85 Wells Ave
Newton, MA 02459

Dear Sir or Madam:

I, _____ (the "Participant"), hereby irrevocably exercise the right to purchase _____ shares of the Common Stock, \$.0001 par value per share (the "Shares"), of Karyopharm Therapeutics Inc. (the "Company") at \$ _____ per share pursuant to the Company's 2013 Stock Incentive Plan and a stock option agreement with the Company dated _____ (the "Option Agreement"). Enclosed herewith is a payment of \$ _____, the aggregate purchase price for the Shares. The certificate for the Shares should be registered in my name as it appears below or, if so indicated below, jointly in my name and the name of the person designated below, with right of survivorship.

Dated:

Signature

Print Name:

Address:

Name and address of persons in whose name the Shares are to be jointly registered (if applicable):

KARYOPHARM THERAPEUTICS INC.
Restricted Stock Unit Agreement (Time Vested) 2013 Stock Incentive Plan

NOTICE OF GRANT

This Restricted Stock Unit Agreement (this “Agreement”) is made as of the Agreement Date between Karyopharm Therapeutics Inc. (the “Company”), a Delaware corporation, and the Participant.

I. Agreement Date and Number

Agreement Date:	
Agreement Number:	

II. Participant Information

Participant:	
Participant Address:	

III. Grant Information

Grant Date:	
Number of Restricted Stock Units:	

IV. Vesting Table

<u>Vesting Date</u>	<u>Number of Restricted Stock Units that Vest</u>
Vest Date Period 1 (MONTH, DD, YYYY)	
Vest Date Period 2 (MONTH, DD, YYYY)	
Vest Date Period 3 (MONTH, DD, YYYY)	
Vest Date Period 4 (MONTH, DD, YYYY)	

This Agreement includes this Notice of Grant and the following Exhibit, which is expressly incorporated by reference in its entirety herein:

Exhibit A – General Terms and Conditions

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the Agreement Date.

By:
Name of Officer: Michael Mason
Title: Chief Financial Officer

Restricted Stock Unit Agreement (Time Vested)
2013 Stock Incentive Plan

EXHIBIT A

GENERAL TERMS AND CONDITIONS

For valuable consideration, receipt of which is acknowledged, the parties hereto agree as follows:

1. Award of Restricted Stock Units.

In consideration of services rendered and to be rendered to the Company by the Participant, the Company has granted to the Participant, subject to the terms and conditions set forth in this Agreement and in the Company's 2013 Stock Incentive Plan (the "Plan"), an award with respect to the number of restricted stock units (the "RSUs") set forth in the Notice of Grant that forms part of this Agreement (the "Notice of Grant"). Each RSU represents the right to receive one share of common stock, \$0.0001 par value per share, of the Company (the "Common Stock") upon vesting of the RSUs, subject to the terms and conditions set forth herein.

2. Vesting.

(a) The RSUs shall vest in accordance with the Vesting Table set forth in the Notice of Grant (the "Vesting Table"). Any fractional shares resulting from the application of any percentages used in the Vesting Table shall be rounded down to the nearest whole number of RSUs (except for the last vesting tranche).

(b) Upon the vesting of the RSUs, the Company will deliver to the Participant, for each RSU that becomes vested, one share of Common Stock, subject to the payment of any withholding taxes pursuant to Section 7. The Common Stock will be delivered to the Participant as soon as practicable following each vesting date, but in any event within 30 days of such date.

3. Forfeiture of Unvested RSUs Upon Cessation of Service.

(a) Except as otherwise provided in Section 3(b) hereof, in the event that the Participant ceases to perform services to the Company for any reason or no reason, with or without Cause (as defined in the Plan), all of the RSUs that are unvested as of the time of such cessation shall be forfeited immediately and automatically to the Company, without the payment of any consideration to the Participant, effective as of such cessation. The Participant shall have no further rights with respect to the unvested RSUs or any Common Stock that may have been issuable with respect thereto. If the Participant provides services to a subsidiary of the Company, any references in this Agreement to provision of services to the Company shall instead be deemed to refer to service with such subsidiary.

- (b) In the event that the Participant's services are terminated by the Company without Cause (as defined in the Plan) within one year following the consummation of a Change in Control Event (as defined in the Plan), all of the RSUs that are unvested and have not been forfeited as of the time of such termination shall immediately vest in full on the Participant's date of termination. Upon the vesting of the RSUs as described in this Section 3(b), the Company will deliver to the Participant, for each RSU that becomes vested, one share of Common Stock, subject to the payment of any taxes pursuant to Section 7. The Common Stock will be delivered to the Participant as soon as practicable following the Participant's date of termination, but in any event within 30 days of such date.

4. Restrictions on Transfer.

The Participant shall not sell, assign, transfer, pledge, hypothecate, encumber or otherwise dispose of, by operation of law or otherwise (collectively "transfer") any RSUs, or any interest therein. The Company shall not be required to treat as the owner of any RSUs or issue any Common Stock to any transferee to whom such RSUs have been transferred in violation of any of the provisions of this Agreement.

5. Rights as a Stockholder.

The Participant shall have no rights as a stockholder of the Company with respect to any shares of Common Stock that may be issuable with respect to the RSUs until the issuance of the shares of Common Stock to the Participant following the vesting of the RSUs.

6. Provisions of the Plan.

This Agreement is subject to the provisions of the Plan, a copy of which is furnished to the Participant with this Agreement.

7. Tax Matters.

- (a) Acknowledgments; No Section 83(b) Election. The Participant acknowledges that he or she is responsible for obtaining the advice of the Participant's own tax advisors with respect to the award of RSUs, and the Participant is relying solely on such advisors and not on any statements or representations of the Company or any of its agents with respect to the tax consequences relating to the RSUs. The Participant understands that the Participant (and not the Company) shall be responsible for the Participant's tax liability that may arise in connection with the acquisition, vesting and/or disposition of the RSUs. The Participant acknowledges that no election under Section 83(b) of the Internal Revenue Code, as amended, is available with respect to RSUs.

- (b) Withholding. The Participant acknowledges and agrees that the Company has the right to deduct from payments of any kind otherwise due to the Participant any federal, state, local or other taxes of any kind required by law to be withheld with respect to the vesting of the RSUs. At such time as the Participant is not aware of any material nonpublic information about the Company or the Common Stock, and the Participant is not otherwise prevented from doing so under the Company's Insider Trading Policy, the Participant shall execute the instruction set forth in Schedule A attached hereto (the "Durable

Automatic Sale Instruction”) as the means of satisfying such tax obligation; provided that once the Participant has executed and delivered such Durable Automatic Sale Instruction to the Company, the Participant shall not be required to execute the instruction again unless and until the Participant has revoked or otherwise terminated the instruction required by the Durable Automatic Sale Instruction. If the Participant does not execute the Durable Automatic Sale Instruction prior to an applicable vesting date, then the Participant agrees that if under applicable law the Participant will owe taxes at such vesting date on the portion of the Award then vested the Company shall be entitled to immediate payment from the Participant of the amount of any tax required to be withheld by the Company. The Company shall not deliver any shares of Common Stock to the Participant until it is satisfied that all required withholdings have been made.

- (c) Reporting. The Participant acknowledges and agrees to comply with all necessary reporting obligations in the Participant’s jurisdiction (in relation to all taxes, social security contributions and any other similar charges) which arise in relation to the RSUs.

8. Miscellaneous.

- (a) Authority of Compensation Committee. In making any decisions or taking any actions with respect to the matters covered by this Agreement, the Compensation Committee shall have all of the authority and discretion, and shall be subject to all of the protections, provided for in the Plan. All decisions and actions by the Compensation Committee with respect to this Agreement shall be made in the Compensation Committee’s discretion and shall be final and binding on the Participant.
- (b) No Right to Continued Service. The Participant acknowledges and agrees that, notwithstanding the fact that the vesting of the RSUs is contingent upon his or her continued service to the Company, this Agreement does not constitute an express or implied promise of continued service relationship with the Participant or confer upon the Participant any rights with respect to a continued service relationship with the Company.
- (c) Section 409A. The RSUs awarded pursuant to this Agreement are intended to be exempt from or comply with the requirements of Section 409A of the Internal Revenue Code and the Treasury Regulations issued thereunder (“Section 409A”). The delivery of shares of Common Stock on the vesting of the RSUs may not be accelerated or deferred unless permitted or required by Section 409A.
- (d) Data Privacy. The Participant hereby explicitly and unambiguously consents to the collection, use and transfer, in electronic or other form, of his or her personal data as described in this Agreement by and among, as applicable, his or her employer or contracting party and the Company for the exclusive purpose of implementing, administering and managing his or her participation in the Plan.

The Participant understands that the Company holds certain personal information about him or her, including, but not limited to, his or her name, home address and telephone number, work location and phone number, date of birth, hire date, details of all RSUs awarded, cancelled,

vested, unvested or outstanding in the Participant's favor, for the purpose of implementing, administering and managing the Plan ("Personal Data"). The Participant understands that Personal Data may be transferred to any third parties assisting in the implementation, administration and management of the Plan, that these recipients may be located in the Participant's country or elsewhere, and that the recipient's country may have different data privacy laws and protections than the Participant's country. The Participant understands that he or she may request a list with the names and addresses of any potential recipients of the Personal Data by contacting his or her local human resources representative. The Participant authorizes the recipients to receive, possess, use, retain and transfer the Personal Data, in electronic or other form, for the purposes of implementing, administering and managing his or her participation in the Plan, including any requisite transfer of such Personal Data as may be required to a broker or other third party with whom the Participant may elect to deposit any Common Stock acquired upon vesting of the RSUs or in connection with the Participant's execution of the Durable Automatic Sale Instruction and the sale of the Participant's Common Stock pursuant to Schedule A. The Participant understands that Personal Data will be held only as long as is necessary to implement, administer and manage his or her participation in the Plan. The Participant understands that he or she may, at any time, view Personal Data, request additional information about the storage and processing of Personal Data, require any necessary amendments to Personal Data or refuse or withdraw the consents herein, in any case without cost, by contacting in writing his or her local human resources representative. The Participant understands, however, that refusing or withdrawing his or her consent may affect his or her ability to participate in the Plan. For more information on the consequences of Participant's refusal to consent or withdrawal of consent, the Participant understands that he or she may contact his or her local human resources representative. For purposes of this Section 8(d), if the Participant provides services to a subsidiary of the Company, any references in this Section 8(d) to the Company shall be deemed to also refer to such subsidiary.

(e) Participant's Acknowledgements. The Participant acknowledges that he or she: (i) has read this Agreement; (ii) has been represented in the preparation, negotiation and execution of this Agreement by legal counsel of the Participant's own choice or has voluntarily declined to seek such counsel; (iii) understands the terms and consequences of this Agreement; (iv) is fully aware of the legal and binding effect of this Agreement; and (v) agrees that in accepting this award, the Participant will be bound by any clawback policy that the Company has in place or may adopt in the future.

(f) Governing Law. This Agreement shall be construed, interpreted and enforced in accordance with the internal laws of the State of Delaware without regard to any applicable conflicts of laws provisions.

I hereby acknowledge that I have read this Agreement, have received and read the Plan, and understand and agree to comply with the terms and conditions of this Agreement and the Plan.

Participant Acceptance

DURABLE AUTOMATIC SALE INSTRUCTION

This Durable Automatic Sale Instruction is being delivered to Karyopharm Therapeutics Inc. (the "Company") by the undersigned on the date set forth below.

I hereby acknowledge that the Company has granted, or may in the future from time to time grant, to me restricted stock units ("RSUs") under the Company's equity incentive plans as in effect from time to time.

I acknowledge that upon the vesting dates applicable to any such RSUs, I will have compensation income equal to the fair market value of the shares of the Company's common stock subject to the RSU that vest on such date and that the Company is required to withhold income and employment taxes in respect of that compensation income on the applicable vesting date.

I desire to establish a process to satisfy such withholding obligation in respect of all RSUs that have been, or may in the future be, granted by the Company to me through an automatic sale of a portion of the shares of the Company's common stock that would otherwise be issued to me on each applicable vesting date, such portion to be in an amount sufficient to satisfy such withholding obligation, with the proceeds of such sale delivered to the Company in satisfaction of such withholding obligation.

I understand that the Company has arranged for the administration and execution of its equity incentive plans and the sale of securities by plan participants thereunder pursuant to an Internet-based platform administered by a third party (the "Administrator") and the Administrator's designated brokerage partner.

Upon any vesting of my RSUs from and after the date of this Durable Automatic Sale Instruction, I hereby appoint the Administrator (or any successor administrator) to automatically sell such number of shares of the Company's common stock issuable with respect to my RSUs that vest as is sufficient to generate net proceeds sufficient to satisfy the Company's minimum statutory withholding obligations with respect to the income recognized by me upon the vesting of the RSUs (based on minimum statutory withholding rates for all tax purposes, including payroll and social security taxes, that are applicable to such income), and the Company shall receive such net proceeds in satisfaction of such tax withholding obligation.

I hereby appoint the Chief Executive Officer, the Chief Financial Officer and the General Counsel, and any of them acting alone and with full power of substitution, to serve as my attorneys in fact to arrange for the sale of shares of common stock in accordance with these durable automatic sale instructions. I agree to execute and deliver such documents, instruments and certificates as may reasonably be required in connection with the sale of the shares of common stock pursuant to these durable automatic sale instructions.

By signing below, I hereby represent to the Company that, as of the date hereof, I am not aware of any material nonpublic information about the Company or its common

stock and that I am not prohibited from entering into these durable automatic sale instructions by the Company's insider trading policy or otherwise. I have structured these automatic sale instructions to constitute a "binding contract" relating to the sale of common stock, consistent with the affirmative defense to liability under Section 10(b) of the Securities Exchange Act of 1934 under Rule 10b5-1(c) promulgated under such Act.

Print Name: _____

Date: _____

KARYOPHARM THERAPEUTICS INC.
NONSTATUTORY STOCK OPTION AGREEMENT

Inducement Grant

Karyopharm Therapeutics Inc. (the "Company") hereby grants the following stock option. The terms and conditions attached hereto are also a part hereof.

Notice of Grant

Name of optionee (the " <u>Participant</u> "):	
Date of this option grant:	
Number of shares of the Company's Common Stock subject to this option (" <u>Shares</u> "):	
Option exercise price per Share:	
Number, if any, of Shares that vest immediately on the grant date:	
Shares that are subject to vesting schedule:	
Vesting Start Date:	
Final Exercise Date:	

Vesting Schedule:

One Year from Vesting Start Date:	
Each Successive month thereafter:	
All vesting is dependent on the Participant remaining an Eligible Participant, as provided herein.	

This option satisfies in full all commitments that the Company has to the Participant with respect to the issuance of stock, stock options or other equity securities.

By:

Name of Officer: Michael Mason
 Title: Chief Financial Officer

KARYOPHARM THERAPEUTICS INC

Nonstatutory Stock Option Agreement
Incorporated Terms and Conditions

1. Grant of Option.

This agreement evidences the grant by the Company, on the grant date (the "Grant Date") set forth in the Notice of Grant that forms part of this agreement (the "Notice of Grant") to the Participant of an option to purchase, in whole or in part, on the terms provided herein, the number of Shares set forth in the Notice of Grant of common stock, \$0.0001 par value per share, of the Company ("Common Stock") at the exercise price per Share set forth in the Notice of Grant. Unless earlier terminated, this option shall expire at 5:00 p.m., Eastern time, on the Final Exercise Date set forth in the Notice of Grant (the "Final Exercise Date").

The option evidenced by this agreement was granted to the Participant pursuant to the inducement grant exception under NASDAQ Stock Market Rule 5635(c)(4), and not pursuant to the Company's 2013 Stock Incentive Plan (the "Plan") or any other equity incentive plan of the Company, as an inducement that is material to the Participant entering into employment with the Company.

It is intended that the option evidenced by this agreement shall not be an incentive stock option as defined in Section 422 of the Internal Revenue Code of 1986, as amended, and any regulations promulgated thereunder (the "Code"). Except as otherwise indicated by the context, the term "Participant", as used in this option, shall be deemed to include any person who acquires the right to exercise this option validly under its terms.

2. Vesting Schedule.

This option will become exercisable ("vest") in accordance with the vesting schedule set forth on the cover page of this agreement (the "Vesting Schedule"). Any fractional shares resulting from the application of any percentages used in the Vesting Table shall be rounded down to the nearest whole number of shares of Common Stock (except for the last vesting tranche).

Notwithstanding the foregoing, to the extent that the Participant is a party to an employment agreement or other agreement with the Company that provides vesting terms that differ from the Vesting Schedule, the terms set forth in such employment agreement or other agreement shall prevail.

The right of exercise shall be cumulative so that to the extent the option is not exercised in any period to the maximum extent permissible it shall continue to be exercisable, in whole or in part, with respect to all Shares for which it is vested until the earlier of the Final Exercise Date or the termination of this option under Section 3 hereof.

3. Exercise of Option.

(a)Form of Exercise. Each election to exercise this option shall be in writing, in the form of the Stock Option Exercise Notice attached as Annex A, signed by the Participant, and received by the Company at its principal office, accompanied by this agreement, or in such other form, which may be electronic, as determined by the Company, together with payment in full of the exercise price and any applicable tax withholding as follows:

(1) in cash or by check, payable to the order of the Company;

(2) except as may otherwise be approved by the Board of Directors of the Company (the "Board"), in its sole discretion, by (i) delivery of an irrevocable and unconditional undertaking by a creditworthy broker to deliver promptly to the Company sufficient funds to pay the exercise price and any required tax withholding or (ii) delivery by the Participant to the Company of a copy of irrevocable and unconditional instructions to a creditworthy broker to deliver promptly to the Company cash or a check sufficient to pay the exercise price and any required tax withholding;

(3) to the extent approved by the Board, in its sole discretion, by delivery (either by actual delivery or attestation) of shares of Common Stock owned by the Participant valued at their fair market value per share of Common Stock as determined by (or in a manner approved by) the Board, provided (i) such method of payment is then permitted under applicable law, (ii) such Common Stock, if acquired directly from the Company, was owned by the Participant for such minimum period of time, if any, as may be established by the Board in its discretion and (iii) such Common Stock is not subject to any repurchase, forfeiture, unfulfilled vesting or other similar requirements;

(4) to the extent approved by the Board in its sole discretion, by delivery of a notice of "net exercise" to the Company, as a result of which the Participant would receive (i) the number of shares underlying the portion of this option being exercised, less (ii) such number of shares as is equal to (A) the aggregate exercise price for the portion of this option being exercised divided by (B) the fair market value (determined by (or in a manner approved by) the Board) on the date of exercise;

(5) to the extent permitted by applicable law and approved by the Board, in its sole discretion, by payment of such other lawful consideration as the Board may determine; or

(6) by any combination of the above permitted forms of payment.

The Participant may purchase less than the number of shares covered hereby, provided that no partial exercise of this option may be for any fractional share.

(b)Continuous Relationship with the Company Required. Except as otherwise provided in this Section 3, this option may not be exercised unless the Participant, at the time he exercises this option, is, and has been at all times since the Grant Date, an employee, director or officer of, or consultant or advisor to, the Company or any other entity the employees, officers, directors, consultants, or advisors of which are eligible to receive option grants under the Plan (an "Eligible Participant").

(c) Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (d) and (e) below, the right to exercise this option shall terminate three months after such cessation (but in no event after the Final Exercise Date), provided that this option shall be exercisable only to the extent that the Participant was entitled to exercise this option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the non-competition or confidentiality provisions of any employment contract, confidentiality and nondisclosure agreement or other agreement between the Participant and the Company, the right to exercise this option shall terminate immediately upon such violation.

(d) Exercise Period Upon Death or Disability. If the Participant dies or becomes disabled (within the meaning of Section 22(e)(3) of the Code) prior to the Final Exercise Date while he is an Eligible Participant and the Company has not terminated such relationship for "cause" as specified in paragraph (e) below, this option shall be exercisable, within one year following the date of death or disability of the Participant, by the Participant (or in the case of death by an authorized transferee), provided that this option shall be exercisable only to the extent that this option was exercisable by the Participant on the date of his or her death or disability, and further provided that this option shall not be exercisable after the Final Exercise Date.

(e) Termination for Cause. If, prior to the Final Exercise Date, the Participant's employment or other relationship with the Company is terminated by the Company for Cause (as defined below), the right to exercise this option shall terminate immediately upon the effective date of such termination. If the Participant is party to an employment or severance agreement with the Company that contains a definition of "cause" for termination of employment or other relationship with the Company, "Cause" shall have the meaning ascribed to such term in such agreement. Otherwise, "Cause" shall have the same meaning as defined in Section 7(c)(1) below.

4. Withholding.

No Shares will be issued pursuant to the exercise of this option unless and until the Participant pays to the Company, or makes provision satisfactory to the Company for payment of, any federal, state or local withholding taxes required by law to be withheld in respect of this option. The Participant must satisfy all applicable federal, state, and local or other income and employment tax withholding obligations before the Company will deliver stock certificates or otherwise recognize ownership of Common Stock under this option. The Company may decide to satisfy the withholding obligations through additional withholding on salary or wages. If the Company elects not to or cannot withhold from other compensation, the Participant must pay the Company the full amount, if any, required for withholding or have a broker tender to the Company cash equal to the withholding obligations. Payment of withholding obligations is due before the Company will issue any shares on exercise of this option or at the same time as payment of the exercise price, unless the Company determines otherwise. If approved by the Board in its sole discretion, a Participant may satisfy such tax obligations in whole or in part by delivery (either by actual delivery or attestation) of shares of Common Stock underlying this option valued at their fair market value (determined by (or in a manner approved by) the Board); provided, however, except as otherwise provided by the Board, that the total tax withholding

where stock is being used to satisfy such tax obligations cannot exceed the Company's minimum statutory withholding obligations (based on minimum statutory withholding rates for federal and state tax purposes, including payroll taxes, that are applicable to such supplemental taxable income), except that, to the extent that the Company is able to retain shares of Common Stock having a fair market value (determined by (or in a manner approved by) the Company) that exceeds the statutory minimum applicable withholding tax without financial accounting implications or the Company is withholding in a jurisdiction that does not have a statutory minimum withholding tax, the Company may retain such number of shares of Common Stock (up to the number of shares having a fair market value equal to the maximum individual statutory rate of tax (determined by (or in a manner approved by) the Company)) as the Company shall determine in its sole discretion to satisfy the tax liability associated with this option. Shares used to satisfy tax withholding requirements cannot be subject to any forfeiture, unfulfilled vesting or other similar requirements.

5. Reporting.

The Participant acknowledges and agrees to comply with all necessary reporting obligations in the Participant's jurisdiction in relation to all taxes, social security contributions and any other similar charges which arise in relation to this option.

6. Transfer Restrictions.

This option may not be sold, assigned, transferred, pledged or otherwise encumbered by the Participant, either voluntarily or by operation of law, except by will or the laws of descent and distribution, and, during the lifetime of the Participant, this option shall be exercisable only by the Participant.

7. Participant's Acknowledgement of Clawback.

The Participant acknowledges that in accepting this award, the Participant will be bound by any clawback policy that the Company has in place or may adopt in the future.

8. Adjustments for Changes in Common Stock and Certain Other Events.

(a) Changes in Capitalization. In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of Common Stock other than an ordinary cash dividend, the number and class of securities and exercise price per share of this option shall be equitably adjusted by the Company in the manner determined by the Board. Without limiting the generality of the foregoing, in the event the Company effects a split of the Common Stock by means of a stock dividend and the exercise price of and the number of shares subject to this option are adjusted as of the date of the distribution of the dividend (rather than as of the record date for such dividend), then the Participant, if he exercises this option between the record date and the distribution date for such stock dividend, shall be entitled to receive, on the distribution date, the stock dividend with respect to the shares of Common Stock acquired upon exercise of this option, notwithstanding

the fact that such shares were not outstanding as of the close of business on the record date for such stock dividend.

(b) Reorganization Events.

(1) A “Reorganization Event” shall mean: (a) any merger or consolidation of the Company with or into another entity as a result of which all of the Common Stock of the Company is converted into or exchanged for the right to receive cash, securities or other property or is cancelled, (b) any transfer or disposition of all of the Common Stock of the Company for cash, securities or other property pursuant to a share exchange or other transaction or (c) any liquidation or dissolution of the Company.

(2) In connection with a Reorganization Event, the Board may take any one or more of the following actions with respect to this option (or any portion thereof) on such terms as the Board determines: (i) provide that this option shall be assumed, or substantially equivalent option shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof), (ii) upon written notice to the Participant, provide that the unvested and/ or unexercised portion of this option will terminate immediately prior to the consummation of such Reorganization Event unless exercised by the Participant within a specified period following the date of such notice, (iii) provide that this option shall become exercisable, realizable, or deliverable, or restrictions applicable to this option shall lapse, in whole or in part prior to or upon such Reorganization Event, (iv) in the event of a Reorganization Event under the terms of which holders of Common Stock will receive upon consummation thereof a cash payment for each share surrendered in the Reorganization Event (the “Acquisition Price”), make or provide for a cash payment to the Participant with respect to this option equal to (A) the number of shares of Common Stock subject to the vested portion of this option (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such Reorganization Event) multiplied by (B) the excess, if any, of (I) the Acquisition Price over (II) the exercise price of this option and any applicable tax withholdings, in exchange for the termination of this option, (v) provide that, in connection with a liquidation or dissolution of the Company, this option shall convert into the right to receive liquidation proceeds (net of the exercise price thereof and any applicable tax withholdings) and (vi) any combination of the foregoing.

(3) For purposes of clause 7(b)(2)(i) above, this option shall be considered assumed if, following consummation of the Reorganization Event, this option confers the right to purchase, for each share of Common Stock subject to this option immediately prior to the consummation of the Reorganization Event, the consideration (whether cash, securities or other property) received as a result of the Reorganization Event by holders of Common Stock for each share of Common Stock held immediately prior to the consummation of the Reorganization Event (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding shares of Common Stock); provided, however, that if the consideration received as a result of the Reorganization Event is not solely common stock of the acquiring or succeeding corporation (or an affiliate thereof), the Company may, with the consent of the acquiring or succeeding corporation, provide for the consideration to be received upon the exercise of this option to consist solely of such number of shares of common stock of the acquiring or succeeding corporation (or an affiliate thereof) that the Board determined to be equivalent in value (as of the date of such determination or another date specified by the Board)

(c) Change in Control Events.

(1) Definitions.

A "Change in Control Event" shall mean:

- (A) the acquisition by an individual, entity or group (within the meaning of Section 13(d)(3) or 14(d)(2) of the Securities Exchange Act of 1934, as amended (the "Exchange Act") (a "Person") of beneficial ownership of any capital stock of the Company if, after such acquisition, such Person beneficially owns (within the meaning of Rule 13d-3 promulgated under the Exchange Act) 50% or more of the combined voting power of the then-outstanding securities of the Company entitled to vote generally in the election of directors (the "Outstanding Company Voting Securities"); provided, however, that for purposes of this subsection (A), the following acquisitions shall not constitute a Change in Control Event: (1) any acquisition directly from the Company or (2) any acquisition by any corporation pursuant to a Business Combination (as defined below) which complies with clauses (x) and (y) of subsection (C) of this definition; or
- (B) such time as the Continuing Directors (as defined below) do not constitute a majority of the Board (or, if applicable, the Board of Directors of a successor corporation to the Company), where the term "Continuing Director" means at any date a member of the Board (x) who was a member of the Board on the date of the grant of this option or (y) who was nominated or elected subsequent to such date by at least a majority of the directors who were Continuing Directors at the time of such nomination or election or whose election to the Board was recommended or endorsed by at least a majority of the directors who were Continuing Directors at the time of such nomination or election; or
- (C) the consummation of a merger, consolidation, reorganization, recapitalization or share exchange involving the Company or a sale or other disposition of all or substantially all of the assets of the Company (a "Business Combination"), unless, immediately following such Business Combination, each of the following two conditions is satisfied: (x) all or substantially all of the

individuals and entities who were the beneficial owners of the Outstanding Company Voting Securities immediately prior to such Business Combination beneficially own, directly or indirectly, more than 50% of the combined voting power of the then-outstanding securities entitled to vote generally in the election of directors of the resulting or acquiring corporation in such Business Combination (which shall include, without limitation, a corporation which as a result of such transaction owns the Company or substantially all of the Company's assets either directly or through one or more subsidiaries) (such resulting or acquiring corporation is referred to herein as the "Acquiring Corporation") in substantially the same proportions as their ownership of the Outstanding Company Voting Securities immediately prior to such Business Combination and (y) no Person beneficially owns, directly or indirectly, 50% or more of the combined voting power of the then-outstanding securities of such corporation entitled to vote generally in the election of directors (except to the extent that such ownership existed prior to the Business Combination); or

(D) the liquidation or dissolution of the Company.

"Good Reason" shall mean the occurrence of any of the following without the Participant's prior written consent: (A) any change in the Participant's position, title or reporting relationship with the Company from and after such Reorganization Event or Change in Control Event that diminishes in any material respect the authority, duties or responsibilities of the Participant as in effect immediately preceding the Reorganization Event or Change in Control Event, as the case may be; provided, however, that a change in the Participant's title or reporting relationship solely due to the Company becoming a division, subsidiary or other similar part of a larger organization following a Reorganization Event or Change in Control Event shall not by itself constitute Good Reason; or (B) any material reduction in the Participant's annual base compensation from and after such Reorganization Event or Change in Control Event, as the case may be. Notwithstanding the foregoing, "Good Reason" shall not be deemed to have occurred unless (x) the Participant provides the Company with written notice that the Participant intends to terminate employment for one of the grounds set forth in subsections (A) or (B) within sixty (60) days of such ground(s) arising, (y) if such ground is capable of being cured, the Company has failed to cure such ground within a period of thirty (30) days from the date of such written notice, and (z) the Participant terminates employment within six (6) months from the date that Good Reason first occurs.

“Cause” shall, for purposes of Section 7 of this agreement, mean the occurrence of any of the following: (A) the Participant’s willful failure to perform in any material respect the Participant’s material duties or responsibilities for the Company, which is not cured within thirty (30) days of written notice thereof to the Participant from the Company; (B) repeated unexplained or unjustified absence from the Company inconsistent with the Participant’s duties and responsibilities for the Company, which continues without explanation or justification after written notice thereof to the Participant from the Company; (C) the Participant’s willful misconduct that causes material and demonstrable monetary or reputational injury to the Company, including, but not limited to, misappropriation or conversion of assets of the Company (other than non-material assets); or (D) the conviction of the Participant of, or the entry of a plea of guilty or *nolo contendere* by the Participant to, any crime involving moral turpitude or any felony.

(2) Notwithstanding the provisions of Section 7(b), this option shall be immediately exercisable in full if, on or prior to the first anniversary of the date of the consummation of the Change in Control Event, the Participant’s employment with the Company or the acquiring or succeeding corporation is terminated for Good Reason by the Participant or is terminated without Cause by the Company or the acquiring or succeeding corporation.

9. Miscellaneous.

(a) No Right to Employment or Other Status. The grant of this option shall not be construed as giving the Participant the right to continued employment or any other relationship with the Company. The Company expressly reserves the right at any time to dismiss or otherwise terminate its relationship with the Participant free from any liability or claim hereunder, except as otherwise expressly provided herein or provided for in the Letter Agreement.

(b) No Rights As Stockholder. Subject to the provisions of this option, the Participant shall not have any rights as a stockholder with respect to any shares of Common Stock to be distributed with respect to this option until becoming the record holder of such shares.

(c) Amendment. The Board may amend, modify or terminate this agreement, including but not limited to, substituting another option of the same or a different type and changing the date of exercise or realization. Notwithstanding the foregoing, the Participant’s consent to such action shall be required unless (i) the Board determines that the action, taking into account any related action, would not materially and adversely affect the Participant, or (ii) the change is permitted under Section 7 and the Letter Agreement.

(d) Acceleration. The Board may at any time provide that this option shall become immediately exercisable in whole or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part, as the case may be.

(e) Conditions on Delivery of Stock. The Company will not be obligated to deliver any shares of Common Stock pursuant to this agreement until (i) all conditions of this agreement have been met to the satisfaction of the Company, (ii) in the opinion of the Company's counsel, all other legal matters in connection with the issuance and delivery of such shares have been satisfied, including any applicable securities laws and regulations and any applicable stock exchange or stock market rules and regulations, and (iii) the Participant has executed and delivered to the Company such representations or agreements as the Company may consider appropriate to satisfy the requirements of any applicable laws, rules or regulations.

(f) Administration by Board. The Board will administer this agreement and may construe and interpret the terms hereof. Subject to the terms and provisions of the Letter Agreement, the Board may correct any defect, supply any omission or reconcile any inconsistency in this agreement in the manner and to the extent it shall deem expedient to carry the Agreement into effect and it shall be the sole and final judge of such expediency. No director or person acting pursuant to the authority delegated by the Board shall be liable for any action or determination relating to or under this agreement made in good faith.

(g) Appointment of Committees. To the extent permitted by applicable law, the Board may delegate any or all of its powers hereunder to one or more committees or subcommittees of the Board (a "Committee"). All references herein to the "Board" shall mean the Board or a Committee to the extent that the Board's powers or authority hereunder have been delegated to such Committee.

(h) Governing Law. This agreement shall be governed by and interpreted in accordance with the laws of the State of Delaware, excluding choice-of-law principles of the law of such state that would require the application of the laws of a jurisdiction other than the State of Delaware.

KARYOPHARM THERAPEUTICS INC.

Stock Option Exercise Notice

Karyopharm Therapeutics Inc.
85 Wells Ave
Newton, MA 02459

Dear Sir or Madam:

I, _____ (the "Participant"), hereby irrevocably exercise the right to purchase _____ shares of the Common Stock, \$.0001 par value per share (the "Shares"), of Karyopharm Therapeutics Inc. (the "Company") at \$ _____ per share and a stock option agreement with the Company dated _____ (the "Option Agreement"). Enclosed herewith is a payment of \$ _____, the aggregate purchase price for the Shares. The certificate for the Shares should be registered in my name as it appears below or, if so indicated below, jointly in my name and the name of the person designated below, with right of survivorship.

Dated:

Signature

Print Name:

Address:

Name and address of persons in whose name the Shares are to be jointly registered (if applicable):

KARYOPHARM THERAPEUTICS INC.

**2020 ISRAELI EQUITY INCENTIVE SUB PLAN
TO THE 2013 STOCK INCENTIVE PLAN**

1.

General.

- 1.1. This 2020 Israeli Equity Incentive Sub Plan (the “**Sub Plan**”) is a sub plan to the 2013 Stock Incentive Plan (the “**Plan**”) of Karyopharm Therapeutics Inc. (the “**Company**”) and sets forth the terms for the grant of Awards (as defined in the Plan) to Israeli Employees or Israeli Non-Employees (as defined below) whose income is taxable in Israel, according to Section 11(e) of the Plan.
- 1.2. The Plan is hereby incorporated by reference and shall be deemed an integral part of this Sub Plan. Without derogating from the provisions of Section 102 and/or Section 3(i) of the Ordinance (as defined below), all the terms and conditions of the Plan shall apply to the grant of Awards to Israeli Employees or Israeli Non-Employees.
- 1.3. The Plan and this Sub Plan shall be interpreted to be compliant with the applicable Israeli laws.
- 1.4. In the event of conflict or inconsistency between this Sub Plan and the Plan, the terms of this Sub Plan shall prevail with respect to the requirements of the Ordinance and ITA pertaining to the grant of Awards to Israeli Employees or Israeli Non-Employees (all as defined below). In all other respects, the terms of the Plan shall prevail.
- 1.5. This Sub Plan shall become effective on the date of its approval by the Board of Directors of the Company (the “**Board**”).

2. Definitions.

Any capitalized terms not specifically defined in this Sub Plan shall have the meaning assigned to it in the Plan.

As used herein, the following definitions shall apply:

- “**Affiliate**” shall mean an “employing company” within the meaning of Section 102(a) of the Ordinance.
- “**Award Agreement**” means a written agreement between the Company and a holder of an Award evidencing the terms and conditions of the grant of such Award. Each Award Agreement shall be subject to the terms and conditions of the Plan and this Sub Plan.
- “**Capital Gain Award**” means a Trustee 102 Award intended to qualify under the capital gain tax treatment in accordance with the provisions of Sections 102(b)(2) and 102(b)(3) of the Ordinance.
- “**Controlling Shareholder**” shall have the meaning ascribed to it in Section 32(9) of the Ordinance as amended from time to time.
- “**Israeli Employee**” means any Israeli employee of the Company's Israeli Affiliate, and any Israeli individual who is serving as a Nose Misra - Office Holder (as such term is defined in the Israeli Companies’ Law, 5759-1999, including directors) of the Company's Israeli Affiliate, but excluding any Controlling Shareholder.
- “**Israeli Non-Employee**” means any Israeli individual or an entity providing services to the Company or its Israeli Affiliate who is not an Israeli Employee.
- “**ITA**” means the Israeli Tax Authority.
- “**Non-Trustee 102 Award**” means an Award granted to an Israeli Employee pursuant to Section 102(c) of the Ordinance, which is not held in trust by a Trustee.
- “**3(i) Award**” means an Award granted pursuant to Section 3(i) of the Ordinance.

- “**Ordinance**” means the Income Tax Ordinance [New Version], 5721, 1961 as now in effect or as hereafter amended.
- “**Ordinary Income Award**” means a Trustee 102 Award intended to qualify under the ordinary income tax treatment in accordance with the provisions of Section 102(b)(1) of the Ordinance.
- “**Section 102**” means Section 102 of the Ordinance and any regulations, rules, orders or procedures promulgated thereunder as now in effect or as hereafter amended.
- “**Trustee**” means any individual or entity appointed by the Company to serve as a trustee and approved by the ITA, all in accordance with the provisions of Section 102(a) of the Ordinance and the regulations thereof.
- “**Trustee 102 Award**” means an Award granted pursuant to Section 102(b) of the Ordinance and held in trust by a Trustee.

3. **Award grants**

- 3.1. **Eligibility.** The persons eligible to receive Awards under this Sub Plan are Israeli Employees and/or Israeli Non-Employees.
- 3.2. **Types of Awards.** The Board shall have the authority to grant an Award under this Sub Plan classified as (i) a Trustee 102 Award, (ii) a Non-Trustee 102 Award or (iii) a 3(i) Award; provided, however, that a Trustee 102 Award and a Non-Trustee 102 Award may only be granted to an Israeli Employee, and a 3(i) Award shall be granted only to an Israeli Non-Employee.
- 3.3. **Trustee 102 Award.**
- The grant of Trustee 102 Awards under this Sub Plan shall be conditioned upon the filing of this Sub Plan, and any other required document including the appointment of the Trustee to the ITA, and the filing of the Company’s Election (as defined below) with the ITA at least thirty (30) days before the first date of grant of Awards under this Sub Plan, or otherwise as permitted by Israeli law. The grant of Trustee 102 Awards shall be in accordance with the terms and conditions of Section 102.
 - The Company may grant at any single time only one type of Trustee 102 Award, either Capital Gain Award or Ordinary Income Award (the “**Election**”). The Company shall file its Election with the ITA. The Election shall apply to any Israeli Employee who has been granted a Trustee 102 Award. The first Election shall become effective as of the date of grant of the first Trustee 102 Award granted under this Sub Plan and shall remain in effect at least until the end of the year following the year during which the Company first granted a Trustee 102 Award. The Company may not be entitled to change its Election at least until the lapse of a year from the end of the year in which the first Trustee 102 Award was granted pursuant to the prior Election.
 - Such Election shall not prevent the Company from granting Non-Trustee 102 Awards to Israeli Employees or 3(i) Award to Israeli Non-Employees simultaneously.
 - All Trustee 102 Awards will be held in trust by a Trustee, as described herein.
- 3.4. **Non-trustee 102 Award.** The granting of a Non-Trustee 102 Award to an Israeli Employee shall be made in accordance with the provisions of Section 102(c) of the

Ordinance. With respect to Non-Trustee 102 Awards or other awards which are deemed as Non-Trustee 102 Awards, in the event of termination of an Israeli Employee's engagement with the Company or any of its Affiliates, then the Israeli Employee shall submit to the Company and/or its Affiliate a security or guarantee for the payment of tax and/or social security and health tax charges due at the time of sale of Non-Trustee 102 Award, all in accordance with the provisions of Section 102.

3.5. 3(i) Award. The Company may grant 3(i) Awards to any person who is an Israeli Non-Employee.

4. **Trustee**.

4.1. Appointment of Trustee. A Trustee shall be appointed by the Board to administer each Trustee 102 Award in accordance with the provisions of Section 102 and pursuant to a written agreement to be entered into between the Trustee and the Company (the "**Trust Agreement**"). Only one trustee shall be appointed to the Sub Plan.

4.2. Grants of Trustee 102 Awards. All Trustee 102 Awards granted under this Sub Plan as well as shares allocated or issued upon the exercise of such Trustee 102 Awards and/or any rights granted with respect to such Trustee 102 Awards, shall be registered and held by the Trustee for the benefit of the Israeli Employee for the requisite period of time as required by Section 102 or any regulations, rules, orders or procedures promulgated thereunder. The holding period of Capital Gain Award shall be 24 months and the holding period of Ordinary Income Award shall be 12 months (the "**Holding Period**"). The Trustee shall be exempt from any liability in respect of any action or decision duly taken in its capacity as a Trustee, provided, however, that the Trustee acted at all times in good faith.

4.3. Grants of 3(i) Awards. The Board may choose to deposit a 3(i) Award with the Trustee. In such event, the Trustee shall hold such 3(i) Award in trust, until exercised by the holder, pursuant to the Company's instructions from time to time.

4.4. Release of Awards. The Trustee shall not release any Trustee 102 Award granted under this Sub Plan as well as shares allocated or issued upon exercise of such Trustee 102 Award and/or any rights granted with respect to such Trustee 102 Award, until all required payments have been fully made: (i) the receipt by the Trustee of an acknowledgment from the ITA that the Israeli Employee has paid any applicable tax due pursuant to the Ordinance, or (ii) the Company has made other arrangements for the deduction of tax at source acceptable to the Trustee.

5. **The Holding Period Requirements**.

5.1. Holding Period Requirements.

a. Trustee 102 Awards may not be sold, transferred, assigned, pledged, given as collateral, or mortgaged (other than through a transfer by operation of applicable law), nor may they be subject of an attachment, power of attorney or transfer deed (other than a power of attorney for the purpose of participation in shareholders meetings or voting such shares) unless Section 102 and/or the regulations, rules, orders or procedures promulgated thereunder and the Plan allow otherwise.

b. With respect to any Awards granted as a Trustee 102 Award, and subject to the provisions of Section 102, an Israeli Employee shall not be entitled to sell or release

from trust any Trustee 102 Award, any share received upon the exercise of any such Trustee 102 Award, until the lapse of the Holding Period and in accordance with Section 102. Notwithstanding the above, if any such sale or release occurs during the Holding Period and results an adverse tax consequences to the Israeli Employee under Section 102, it shall apply to and shall be borne solely by such Israeli Employee.

- 5.2. **Trustee 102 Award Requirements.** In the event that the requirements of Section 102 with respect to a Trustee 102 Award are not met, then it shall be treated in accordance with the provisions of Section 102 and any regulations promulgated thereunder.
- 5.3. **Award Agreement.** Upon receipt of a Trustee 102 Award, an Israeli Employee shall sign an Award Agreement under which the Israeli Employee shall, among others, (i) agree to be subject to the trust agreement between the Company and the Trustee; (ii) declare that he/she understands the provisions of Section 102, the Plan and this Sub Plan, and the applicable tax track applies to the Trustee 102 Award and approve the applicable tax arrangement; and (iii) confirm that he/she shall neither sell nor transfer the Trustee 102 Award from the Trustee until the lapse of the Holding Period.

6. **Dividends.**

Any dividends payable with respect to shares acquired upon exercise of an Award issued under this Sub Plan and the Plan shall also be subject to the provisions of Section 102 and the rules, regulations or orders promulgated thereunder.

7. **Tax Consequences.**

7.1. **Israeli Employee.**

- a. Any tax consequences arising from the grant of an Award or the exercise of such Award or from the sale or release or transfer of such Award (including, without limitation, the Israeli Employee's social security taxes and health tax, if applicable) or from any other event or act (of the Company and/or its Affiliate, the Trustee or the Israeli Employee), shall be borne solely by the Israeli Employee. Notwithstanding the foregoing, the Company and/or its Affiliate and/or the Trustee shall withhold taxes according to the requirements of the laws, rules, and regulations, including withholding taxes at source under Section 102.
- b. Furthermore, the Israeli Employee shall indemnify the Company and/or Affiliate that employs the Israeli Employee and/or the Company's shareholders and/or directors and/or officers if applicable, and hold them harmless against and from any and all liability for any such tax or interest or penalty thereon, including without limitation, liabilities relating to the necessity to withhold, or to have withheld, any such tax from any payment made to the Israeli Employee.
- c. The Company shall not be obligated to honor the exercise of any Award by or on behalf of an Israeli Employee until all tax consequences (if any) arising from the exercise of such Awards are resolved to the full satisfaction of the Company. Without derogating from the above, the Company and/or the Trustee, when applicable, shall not be required to release any share certificate to an Israeli Employee until all required payments (including tax payments) have been fully made in accordance with Section 102.

- 7.2. Israeli non-employee. Any tax consequences arising from the grant or exercise of Awards to an Israeli Non-Employee, or from the sale or transfer of such Awards or from any other event or act (of the Company and/or its Affiliate or the Israeli Non-Employee), shall be borne solely by the Israeli Non-Employee.

**KARYOPHARM THERAPEUTICS INC.
2020 Israeli Equity Incentive Sub Plan to the 2013 Stock Incentive Plan
Option Agreement**

NOTICE OF GRANT

Karyopharm Therapeutics Inc. (the “Company.”) hereby grants the following stock option pursuant to the 2020 Israeli Equity Incentive Sub Plan to the 2013 Stock Incentive Plan.

Name of optionee (the “ <u>Participant</u> ”):	
Date of this option grant:	
Number of shares of the Company’s Common Stock subject to this option (“ <u>Shares</u> ”):	
Option exercise price per Share:	
Number, if any, of Shares that vest immediately on the grant date:	
Shares that are subject to vesting schedule:	
Vesting Start Date:	
Final Exercise Date:	

Vesting Schedule:

One Year from Vesting Start Date:	
Each Successive month thereafter:	
Four Years from Vesting Start Date:	
All vesting is dependent on the Participant remaining an Eligible Participant, as provided herein.	

This Agreement includes this Notice of Grant and the following Exhibit, which is expressly incorporated by reference in its entirety herein:

Exhibit A – General Terms and Conditions

This option satisfies in full all commitments that the Company has to the Participant with respect to the issuance of stock, stock options or other equity securities.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the Agreement Date.

KARYOPHARM THERAPEUTICS INC.

By:
Name of Officer: Michael Mason
Title: Chief Financial Officer

KARYOPHARM THERAPEUTICS INC.
2020 Israeli Equity Incentive Sub Plan to the 2013 Stock Incentive Plan
Option Agreement
Exhibit A

GENERAL TERMS AND CONDITIONS

1. Grant of Option.

This agreement evidences the grant by the Company, on the grant date (the "Grant Date") set forth in the Notice of Grant that forms part of this agreement (the "Notice of Grant"), to the Participant, an employee of the Company, of an option to purchase, in whole or in part, on the terms provided herein and in the Company's 2020 Israeli equity incentive sub plan (the "Sub Plan") to the 2013 Stock Incentive Plan (the "Plan"), the number of shares set forth in the Notice of Grant of common stock, \$0.0001 par value per share, of the Company ("Common Stock") at the exercise price per Share set forth in the Notice of Grant (the "Option"). Unless earlier terminated, this Option shall expire at 5:00 p.m., Eastern time, on the Final Exercise Date set forth in the Notice of Grant (the "Final Exercise Date").

It is intended that the Option evidenced by this agreement shall be awarded in accordance with Section 102(b)(2) of the Israeli Income Tax Ordinance [New Version], 5721, 1961 as now in effect or as hereafter amended, and any regulations promulgated thereunder (the "Ordinance"). Except as otherwise indicated by the context, the term "Participant", as used in this Award Agreement, shall be deemed to include any Israeli Employee of the Company or the Company's Affiliate (as defined in the Sub Plan) who acquires the right to exercise this Option validly under its terms.

2. Vesting Schedule.

This Option will become exercisable ("vest") in accordance with the vesting schedule set forth on the cover page of this agreement (the "Vesting Schedule"). Any fractional shares resulting from the application of any percentages used in the Vesting Table shall be rounded down to the nearest whole number of shares of Common Stock (except for the last vesting tranche).

Notwithstanding the foregoing, to the extent that the Participant is a party to an employment agreement or other agreement with the Company or the Company's Affiliate, that provides vesting terms that differ from the Vesting Schedule, the terms set forth in such employment agreement or other agreement shall prevail.

The right of exercise shall be cumulative so that to the extent the Option is not exercised in any period to the maximum extent permissible it shall continue to be exercisable, in whole or in part, with respect to all shares for which it is vested until the earlier of the Final Exercise Date or the termination of this Option under this Agreement, the Sub Plan or the Plan.

3. Exercise of Option.

a) Form of Exercise. Each election to exercise this option shall be in writing, in the form of the Stock Option Exercise Notice attached as Annex A, signed by the Participant, and received by the Company at its principal office, accompanied by this agreement, or in such other form, which may be electronic, as determined by the Company, together with payment in full of the exercise price and any applicable tax withholding in the manner provided in the Plan. The Participant may purchase less than the number of shares covered hereby, provided that no partial exercise of this Option may be for any fractional share.

b) Continuous Relationship with the Company Required. Except as otherwise provided in this Section 3, the Option may not be exercised unless the Participant, at the time he or she exercises this Option, is, and has been at all times since the Grant Date, an Israeli Employee of the Company or the Company's Affiliate (as defined in the Sub Plan) (an "Eligible Participant").

c) Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (d) and (e) below, the right to exercise this Option shall terminate three months after such cessation (but in no event after the Final Exercise Date), provided that this Option shall be exercisable only to the extent that the Participant was entitled to exercise this Option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the non-competition or confidentiality provisions of any employment contract, confidentiality and nondisclosure agreement or other agreement between the Participant and the Company, the right to exercise this Option shall terminate immediately upon such violation.

d) Exercise Period Upon Death or Disability. If the Participant dies or becomes disabled (within the meaning of Section 22(e)(3) of the U.S. Internal Revenue Code of 1986) prior to the Final Exercise Date while he or she is an Eligible Participant and the Company has not terminated such relationship for "Cause" as specified in paragraph (e) below, this Option shall be exercisable, within one year following the date of death or disability of the Participant, by the Participant (or in the case of death by an authorized transferee), provided that this Option shall be exercisable only to the extent that this Option was exercisable by the Participant on the date of his or her death or disability, and further provided that this Option shall not be exercisable after the Final Exercise Date.

e) Termination for Cause. If, prior to the Final Exercise Date, the Participant's employment is terminated by the Company for Cause (as defined below), the right to exercise this Option shall terminate immediately upon the effective date of such termination of employment. "Cause" shall mean, in the good faith determination of the Company, that the Participant has: (i) committed gross negligence or willful malfeasance in the performance of the Participant's work or duties; (ii) committed a breach of fiduciary duty or a breach of any non-competition, non-solicitation or confidentiality obligations to the Company; (iii) failed to follow the proper directions of the Participant's direct or indirect supervisor after written notice of such failure; (iv) been convicted of, or pleaded "guilty" or "no contest" to, any misdemeanor relating to the affairs of the Company and its Affiliate or any felony; (v) disregarded the material rules or material policies of the Company and its Affiliate which has not been cured within 15 days after notice thereof from the Company; or (vi) engaged in intentional acts that have generated material adverse publicity toward or about the Company and its Affiliate.

4. Tax Matters.

a) Withholding. No Shares will be issued pursuant to the exercise of this Option unless and until the Participant pays to the Company or its Affiliate, or makes provision satisfactory to the Company for payment of, any national, state or local withholding taxes required by law to be withheld in respect of this Option.

b) Reporting. The Participant acknowledges and agrees to comply with all necessary reporting obligations in the Participant's jurisdiction in relation to all taxes, social security contributions and any other similar charges which arise in relation to this Option.

5. Transfer Restrictions.

This Option may not be sold, assigned, transferred, pledged or otherwise encumbered by the Participant, either voluntarily or by operation of law, except by the applicable laws of descent and distribution, and, during the lifetime of the Participant, this Option shall be exercisable only by the Participant.

6. Provisions of the Plan.

a) This Option is subject to the provisions of the Sub Plan and the Plan (including the provisions relating to amendments to the Sub Plan and the Plan), a copy of which is furnished to the Participant with this Option.

b) Participant acknowledges receipt of a copy of the Sub Plan, the Plan and the Trust Agreement (as defined below) and represents that he or she is familiar with the terms and provisions thereof, and hereby accepts that this Option is subject to all of the terms and provisions thereof.

7. Participant's Acknowledgement of Clawback.

The Participant acknowledges that in accepting this award, the Participant will be bound by any clawback policy that the Company has in place or may adopt in the future.

8. Compliance with Israeli law

a) This Award Agreement is subject to Section 102 of the Ordinance and any tax rulings the Company shall obtain from the ITA (as defined in the Sub Plan). Appointment of the Trustee (as defined below) and the Sub Plan shall be subject to the required procedure of the ITA and its approval (if applicable).

b) The Option granted to Participant under this Award Agreement will be held by a trustee (the "Trustee"), pursuant to the trust agreement executed between the Company and the Trustee (the "Trust Agreement"). The Trustee will hold the Option (and the Shares issued upon exercise of the Option) in accordance with the Trust Agreement, the Sub Plan, the Plan, Section 102 and any applicable laws, and withhold any tax due (including National Insurance and health tax if applicable) in accordance with the terms and conditions of Section 102 and any applicable laws. The Participant shall indemnify the Company and/or its shareholders and/or its Affiliates and/or its officers, and hold them harmless against and from any and all liability for any such tax or interest or penalty thereon, including without limitation, liabilities relating to withholding tax.

NO SHARES SHALL BE ISSUED PURSUANT TO THE EXERCISE OF AN OPTION UNLESS SUCH ISSUANCE AND SUCH EXERCISE COMPLY WITH APPLICABLE LAWS.

c) Upon exercise of the Option the Shares shall be held issued and registered in the name of the Trustee for the benefit of the Participant, in accordance with Section 102.

d) Participant shall not be entitled to sell or release from trust any Option and/or shares issued upon the exercise of Option (or any other property received with respect to such shares) until the lapse of the Holding Period in accordance with Section 102. Notwithstanding the foregoing, if any such sale or release occurs during the Holding Period, the tax sanctions and considerations set forth under Section 102 (including national insurance and health tax) shall apply to and shall be borne solely by Participant. In such event, the Trustee and/or the Company shall make any withholding required pursuant to applicable laws.

e) During the Holding Period, no Option or shares issued upon exercise of the Option or any right with respect thereto, shall be assignable, transferable, pledged, mortgaged, or given as collateral, and no right with respect to such an Option and/or shares may be given to any third party whatsoever, all in accordance with Section 102.

f) As of the Final Exercise Date, all unexercised Options (whether or not vested) shall terminate and have no further affect, unless earlier terminated.

g) This Award Agreement, the Sub Plan and the Plan together constitute the entire agreement and supersede all prior understandings and agreements, written or oral, of the parties hereto with respect to the subject matter hereof.

h) If a court of competent jurisdiction determines that any portion of this Award Agreement, the Sub Plan, the Plan or the Exercise Notice is in violation of any statute or public policy, then only the portions of this Award Agreement, the Sub Plan, the Plan or the Exercise Notice, as applicable, which violate such statute or public policy shall be stricken, and all portions of this Award Agreement, the Sub Plan, the Plan and the Exercise Notice, which do not violate any statute or public policy shall continue in full force and effect. Furthermore, it is the parties' intent that any court order striking any portion of this Award Agreement, the Sub Plan, the Plan and/or the Exercise Notice should modify the stricken terms as narrowly as possible to give as much effect as possible to the intentions of the parties hereunder.

IN WITNESS WHEREOF, this Award Agreement has been executed by each party on the date indicated below, respectively.

KARYOPHARM THERAPEUTICS INC.

By: _____
Name: _____
Title: _____
Date: _____

After having an adequate opportunity to review the above terms, including the Sub Plan, the Plan and the Trust Agreement and seek advice of legal counsel, I, the undersigned Participant, hereby declare, agree to and accept all of the terms and conditions of this Award Agreement, Sub Plan, Plan and Trust Agreement. I, the undersigned Participant, hereby further declare and acknowledge, by my signature below that I: (i) fully understand Section 102, the rules and regulations promulgated thereunder apply to the Option specified in this Award Agreement; (ii) understand the tax track chosen and the implications thereof; (iii) understand that the Option shall also be subject to the terms of the Trust Agreement; and (iv) shall neither sell nor transfer the Option until the lapse of the Holding Period.

By: _____

Date: _____

ANNEX A

KARYOPHARM THERAPEUTICS INC.
Stock Option Exercise Notice

Karyopharm Therapeutics Inc.
85 Wells Avenue
Newton, MA 02459

Dear Sir or Madam:

1. I, (the "Participant"), hereby irrevocably exercise the right to purchase shares of the Common Stock, \$.0001 par value per share (the "Shares"), of Karyopharm Therapeutics Inc. (the "Company") at \$ per share pursuant to the Company's 2020 Israeli Equity Incentive Sub Plan (the "Sub Plan") to the 2013 Stock Incentive Plan (the "Plan") and the Award agreement with the Company dated (the "Award Agreement"). Enclosed herewith is a payment of \$, the aggregate purchase price for the Shares.
2. Notwithstanding the exercise of any Option, until the issuance of the Shares (as evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company), no right to receive dividends or any other rights as a shareholder shall exist with respect to the Shares. The Shares shall be held issued and registered in the name of the Trustee for the benefit of the Participant in accordance with Section 102. The Trustee will transfer the Shares to Participant upon demand subject to all applicable tax laws and any other restrictions specified in the Sub Plan and under applicable laws including Section 102. No adjustment shall be made for a dividend or other right for which the record date is prior to the date of issuance, unless approved by the Board.
3. Upon issuance of the Shares, the holder of the Shares shall be subject to all rights and obligations as set forth in the Sub Plan, the Plan, Company's Restated Certificate of Incorporation, shareholders agreements, voting agreements or any other relevant agreement, as may be amended from time to time, all in accordance with the instructions then issued by the Company's Board of Directors.
4. Participant understands that he/she may suffer adverse tax consequences as a result of Participant's purchase or sale of the Shares. Participant represents that he/she has consulted with his/her tax consultants as Participant deems advisable in connection with the purchase or sale of the Shares and that Participant is not relying on the Trustee and/or the Company or their representatives for any tax advice.
5. The Company may assign any of its rights under the Award Agreement to single or multiple assignees, and the Award Agreement shall inure to the benefit of the successors and assigns of the Company.
6. Any dispute regarding the interpretation of this Exhibit shall be submitted by Participant or by the Company forthwith to the Board which shall review such dispute at its next regular meeting. The resolution of such a dispute by the Board shall be final and binding on all parties.
7. The Sub Plan, the Plan, the Award Agreement including its Exhibits and the Trust Agreement constitute the entire agreement of the parties with respect to the subject matter hereof and supersede in their entirety all prior undertakings and agreements of the Company and Participant with respect to the subject matter hereof.

Dated:

Signature

Print Name:

Address:

Name and address of persons in whose name the Shares are to be jointly registered (if applicable):

KARYOPHARM THERAPEUTICS INC.
2020 Israeli Equity Incentive Sub Plan to the 2013
Stock Incentive Plan
Restricted Stock Unit Agreement (Time Vested)
Exhibit A

GENERAL TERMS AND CONDITIONS

For valuable consideration, receipt of which is acknowledged, the parties hereto agree as follows:

1. Award of Restricted Stock Units.

In consideration of the Participant's employment, the Company has granted to the Participant, subject to the terms and conditions set forth in this Agreement and in the Company's 2020 Israeli Equity Incentive Sub Plan (the "Sub Plan") to the Company's 2013 Stock Incentive Plan (the "Plan"), an award with respect to the number of restricted stock units (the "RSUs") set forth in the Notice of Grant that forms part of this Restricted Stock Unit Agreement (the "Notice of Grant"). Each RSU represents the right to receive one share of common stock, \$0.0001 par value per share, of the Company (the "Common Stock") upon vesting of the RSU, subject to the terms and conditions set forth herein.

It is intended that the RSUs evidenced by this agreement shall be awarded subject to and in accordance with Section 102(b)(2) of the Israeli Income Tax Ordinance [New Version], 5721, 1961 as now in effect or as hereafter amended, and any regulations promulgated thereunder (the "Ordinance"), (Capital Gain Award as defined in the Sub-Plan).

2. Vesting.

- (a) The RSUs shall vest in accordance with the Vesting Table set forth in the Notice of Grant (the "Vesting Table"). Any fractional shares resulting from the application of any percentages used in the Vesting Table shall be rounded down to the nearest whole number of RSUs (except for the last vesting tranche).
- (b) Upon the vesting of the RSUs, the Company will deliver to the Trustee (as defined in the Sub Plan), for each RSU that becomes vested, one share of Common Stock, subject to the payment of any withholding taxes pursuant to Section 7 (if applicable). The Common Stock will be delivered as soon as practicable following each vesting date, but in any event within 30 days of such date.
3. Forfeiture of Unvested RSUs Upon Termination of Employment.

- (a) Except as otherwise provided in Section 3(b) hereof, in the event that the Participant ceases to be employed by the Company for any reason or no reason, with or without Cause (as defined in the Plan), all of the RSUs that are unvested as of the time of such cessation

shall be forfeited immediately and automatically to the Company, without the payment of any consideration to the Participant, effective as of such cessation. The Participant shall have no further rights with respect to the unvested RSUs or any Common Stock that may have been issuable with respect thereto. If the Participant is employed by a subsidiary of the Company, any references in this Agreement to employment by the Company shall instead be deemed to refer to such subsidiary.

- (b) In the event that the Participant's employment is terminated by the Company without Cause (as defined in the Plan) within one year following the consummation of a Change in Control Event (as defined in the Plan), all of the RSUs that are unvested and have not been forfeited as of the time of such termination shall immediately vest in full on the Participant's date of termination. Upon the vesting of the RSUs as described in this Section 3(b), the Company will deliver to the Trustee, for each RSU that becomes vested, one share of Common Stock, subject to the payment of any taxes pursuant to Section 7. The Common Stock will be delivered as soon as practicable following the Participant's date of termination, but in any event within 30 days of such date.

4. Restrictions on Transfer.

The Participant shall not sell, assign, transfer, pledge, hypothecate, encumber or otherwise dispose of, by operation of law or otherwise (collectively "transfer") any RSUs, or any interest therein. The Company shall not be required to treat as the owner of any RSUs or issue any Common Stock to any transferee to whom such RSUs have been transferred in violation of any of the provisions of this Agreement.

5. Rights as a Stockholder.

The Participant shall have no rights as a stockholder of the Company with respect to any shares of Common Stock that may be issuable with respect to the RSUs until the issuance of the shares of Common Stock following the vesting of the RSUs.

6. Provisions of the Plan and the Sub Plan.

This Agreement is subject to the provisions of the Plan and the Sub Plan (a copy of which is furnished to the Participant with this Agreement).

7. Tax Matters.

- (a) Acknowledgments: The Participant acknowledges that he or she is responsible for obtaining the advice of the Participant's own tax advisors with respect to the award of RSUs, and the Participant is relying solely on such advisors and not on any statements or representations of the Company or any of its agents with respect to the tax consequences relating to the RSUs. The Participant understands that the Participant (and not the Company) shall be responsible for the Participant's tax liability that may arise in connection with the acquisition, vesting and/or disposition of the RSUs.

- (b) Withholding. The Participant acknowledges and agrees that the Company has the right to deduct from payments of any kind otherwise due to the Participant any federal, state, local, Israeli or other taxes of any kind required by law to be withheld with respect to the vesting of the RSUs. The Participant shall indemnify the Company and/or its

shareholders and/or its Affiliates and/or its officers, and hold them harmless against and from any and all liability for any such tax or interest or penalty thereon, including without limitation, liabilities relating to withholding tax.

- (c) Reporting. The Participant acknowledges and agrees to comply with all necessary reporting obligations in the Participant's jurisdiction (in relation to all taxes, social security contributions and any other similar charges) which arise in relation to the RSUs.

8. Miscellaneous.

- (a) Authority of Compensation Committee. In making any decisions or taking any actions with respect to the matters covered by this Agreement, the Compensation Committee or the Board shall have all of the authority and discretion, and shall be subject to all of the protections, provided for in the Plan. All decisions and actions by the Compensation Committee or the Board with respect to this Agreement shall be made in the Compensation Committee's or the Board's discretion and shall be final and binding on the Participant.
- (b) No Right to Continued Employment. The Participant acknowledges and agrees that, notwithstanding the fact that the vesting of the RSUs is contingent upon his or her continued employment in the Company, this Agreement does not constitute an express or implied promise of continued employment or confer upon the Participant any rights with respect to a continued employment in the Company.
- (c) No Right to Accelerate or Defer. The delivery of shares of Common Stock on the vesting of the RSUs may not be accelerated or deferred unless permitted or required by the Ordinance.
- (d) Data Privacy. The Participant hereby explicitly and unambiguously consents to the collection, use and transfer, in electronic or other form, of his or her personal data as described in this Agreement by and among, as applicable, his or her employer or contracting party and the Company for the exclusive purpose of implementing, administering and managing his or her participation in the Plan and the Sub Plan.

The Participant understands that the Company holds certain personal information about him or her, including, but not limited to, his or her name, home address and telephone number, work location and phone number, date of birth, hire date, details of all RSUs awarded, cancelled, vested, unvested or outstanding in the Participant's favor, for the purpose of implementing, administering and managing the Plan ("Personal Data"). The Participant understands that Personal Data may be transferred to any third parties assisting in the implementation, administration and management of the Plan and the Sub Plan, that these recipients may be located in the Participant's country or elsewhere, and that the recipient's country may have different data privacy laws and protections than the Participant's country. The Participant understands that he or she may request a list with the names and addresses of any potential recipients of the Personal Data by contacting his or her local human resources representative. The Participant authorizes the recipients to receive, possess, use, retain and transfer the Personal Data, in electronic or other form, for the purposes of implementing, administering and managing his or her participation in the Plan, including any requisite transfer of such Personal Data as may be required to a broker or other third party with whom the Participant may elect to deposit any Common Stock acquired upon vesting of the RSUs and the sale of the Participant's Common

Stock. The Participant understands that Personal Data will be held only as long as is necessary to implement, administer and manage his or her participation in the Plan. The Participant understands that he or she may, at any time, view Personal Data, request additional information about the storage and processing of Personal Data, require any necessary amendments to Personal Data or refuse or withdraw the consents herein, in any case without cost, by contacting in writing his or her local human resources representative. The Participant understands, however, that refusing or withdrawing his or her consent may affect his or her ability to participate in the Plan. For more information on the consequences of Participant's refusal to consent or withdrawal of consent, the Participant understands that he or she may contact his or her local human resources representative. For purposes of this Section 8(d), if the Participant is employed by a subsidiary of the Company, any references in this Section 8(d) to the Company shall be deemed to also refer to such subsidiary.

- (e) Participant's Acknowledgements. The Participant acknowledges that he or she: (i) has read this Agreement, the Plan and the Sub Plan; (ii) has been represented in the preparation, negotiation and execution of this Agreement by legal counsel and tax advisor of the Participant's own choice or has voluntarily declined to seek such counsel/advisor; (iii) understands the terms and consequences of this Agreement; (iv) is fully aware of the legal and binding effect of this Agreement; and (v) agrees that in accepting this Award, the Participant will be bound by any clawback policy that the Company has in place or may adopt in the future.

- (f) Governing Law. This Agreement shall be construed, interpreted and enforced in accordance with the laws of the State of Israel without regard to any applicable conflicts of laws provisions.

IN WITNESS WHEREOF, this Award Agreement has been executed by each party on the date indicated below, respectively.

KARYOPHARM THERAPEUTICS INC.

By: _____
Name: _____
Title: _____
Date: _____

After having an adequate opportunity to review the above terms, including the Sub Plan, the Plan and the Trust Agreement and seek advice of legal counsel, I, the undersigned Participant, hereby declare, agree to and accept all of the terms and conditions of this Award Agreement, Sub Plan, Plan and Trust Agreement. I, the undersigned Participant, hereby further declare and acknowledge, by my signature below, that I: (i) fully understand Section 102, the rules and regulations promulgated thereunder apply to the award of Restricted Stock Units specified in this Award Agreement; (ii) understand the tax track chosen and the implications thereof; and (iii) understand that this Award shall also be subject to the terms of the Trust Agreement.

By: _____
Date: _____

CERTIFICATIONS

I, Michael Kauffman, M.D., Ph.D., 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 KAUFFMAN

Michael Kauffman, M.D., Ph.D.
Chief Executive Officer
(Principal executive officer)

Date: November 2, 2020

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

*Senior Vice President, Chief Financial Officer and Treasurer
(Principal financial and accounting officer)*

Date: November 2, 2020

**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 September 30, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Michael Kauffman, M.D., Ph.D., 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/ MICHAEL KAUFFMAN

Michael Kauffman, M.D., Ph.D.
Chief Executive Officer
(Principal executive officer)

Date: November 2, 2020

**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 September 30, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Michael Mason, Senior 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

*Senior Vice President, Chief Financial Officer and Treasurer
(Principal financial and accounting officer)*

Date: November 2, 2020