

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, DC 20549**

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**FORM 8-K**

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**CURRENT REPORT  
Pursuant to Section 13 or 15(d)  
of the Securities Exchange Act of 1934**

**Date of report (Date of earliest event reported): December 7, 2019**

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**Karyopharm Therapeutics Inc.**  
(Exact Name of Registrant as Specified in Charter)

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**Delaware**  
(State or Other Jurisdiction  
of Incorporation)

**001-36167**  
(Commission  
File Number)

**26-3931704**  
(IRS Employer  
Identification No.)

**85 Wells Avenue, 2nd Floor  
Newton, Massachusetts**  
(Address of Principal Executive Offices)

**02459**  
(Zip Code)

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

(Former Name or Former Address, if Changed Since Last Report)

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Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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

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

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

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

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**Item 8.01 Other Events.**

On December 7, 2019, Karyopharm Therapeutics Inc. (the “Company”) issued a press release announcing that two presentations highlighting new and updated data relating to XPOVIO® (selinexor), the Company’s first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound, will be given at the American Society of Hematology 2019 Annual Meeting (the “ASH Annual Meeting”) taking place December 7-10 in Orlando.

On December 8, 2019, the Company issued a press release announcing that four posters relating to XPOVIO and eltanexor, its next generation SINE compound, will be presented at the ASH Annual Meeting.

Copies of the press releases are filed as Exhibit 99.1 and 99.2, respectively, to this Current Report on Form 8-K and are incorporated herein by reference.

**Item 9.01 Financial Statements and Exhibits.****(d) Exhibits**

99.1 [Press release issued by Karyopharm Therapeutics Inc. on December 7, 2019.](#)

99.2 [Press release issued by Karyopharm Therapeutics Inc. on December 8, 2019.](#)

104 Cover Page Interactive Data File (formatted as Inline XBRL)

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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 hereunto duly authorized.

Date: December 9, 2019

KARYOPHARM THERAPEUTICS INC.

By: /s/ Christopher B. Primiano  
Christopher B. Primiano  
Executive Vice President, Chief Business Officer, General Counsel  
and Secretary



**Karyopharm Reports New and Updated XPOVIO® (Selinexor) Data in Relapsed or Refractory Multiple Myeloma at the American Society of Hematology 2019 Annual Meeting**

- *All Oral Regimen of Once Weekly Selinexor in Combination with Daily Pomalyst® and Low Dose Dexamethasone Demonstrates 56% Overall Response Rate in Pomalyst®-Naïve and Revlimid®-Relapsed or -Refractory Myeloma with Progression-Free Survival of 12.2 Months —*
- *Selinexor and Low Dose Dexamethasone Either Alone or in Combination with Velcade® or Kyprolis® Results in Responses in Six of Seven Patients Whose Myeloma Has Progressed Following Experimental CAR-T Therapy —*

**NEWTON, Mass.** – December 7, 2019 – Karyopharm Therapeutics Inc. (Nasdaq:KPTI), an oncology-focused pharmaceutical company, today announced that two presentations highlighting new and updated data relating to XPOVIO® (selinexor), the Company’s first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound, will be given at the American Society of Hematology (ASH) 2019 Annual Meeting taking place December 7-10, 2019 in Orlando. The first study, which will be featured in an oral presentation, describes updated data from the Phase 1b/2 STOMP study evaluating the all oral regimen of selinexor in combination with Pomalyst® (pomalidomide) and low-dose dexamethasone (dex) (SPd) in patients with relapsed or refractory multiple myeloma. The second abstract, which will be featured in a poster presentation, describes new data on the use of selinexor and dexamethasone, either alone or in combination with standard approved therapies, in patients with multiple myeloma whose disease has progressed following experimental chimeric antigen receptor T-cell (CAR-T) therapy.

“We continue to be pleased with the efficacy and safety observed in the all oral selinexor plus Pomalyst arm of the Phase 1b/2 STOMP study, where patients with Pomalyst-naïve and Revlimid® (lenalidomide)-relapsed or -refractory myeloma achieved a 56% overall response rate (ORR) and a 12-month progression free survival (PFS),” said Sharon Shacham, PhD, MBA, Founder, President and Chief Scientific Officer of Karyopharm. “Another key study this year is the presentation of new data from patients treated with selinexor-based regimens after their myeloma had progressed following experimental CAR-T therapy. Although these data are early, six of seven patients whose disease relapsed after CAR-T achieved a response when treated with selinexor and dexamethasone alone or in combination with either Velcade® (bortezomib) or Kyprolis® (carfilzomib). There is currently very limited data regarding treatment options for patients whose disease has progressed following experimental CAR-T therapy, and we believe these encouraging results further reinforce the therapeutic activity of selinexor in patients with relapsed or refractory disease.”

**Updated Data from Phase 1b/2 STOMP Study Evaluating Selinexor in Combination with Pomalyst and Low-dose Dexamethasone (SPd)**

In this arm of the Phase 1b/2 STOMP study, oral selinexor is being evaluated in combination with Pomalyst (3 or 4mg orally, once daily) and low dose dexamethasone (orally, 40mg once weekly or 20mg twice weekly) in patients with relapsed or refractory multiple myeloma who received at least three prior lines of therapy, including a proteasome inhibitor (PI) and an immunomodulatory drug (IMiD), or patients with myeloma refractory to both a PI and an IMiD. The following table is a summary of the efficacy results:

**Best Responses<sup>1</sup> in Evaluable SPd Patients as of 1-Oct-2019<sup>2</sup>**

Prior Therapy Status	N <sup>3</sup>	ORR	VGPR <sup>4</sup>	PR	Median PFS
Pomalyst-naïve and Revlimid refractory or relapsed	32	18 (56%)	6 (19%)	12 (38%)	12.2 months
Pomalyst Treated and Revlimid refractory	14	5 (36%)	1 (7%)	4 (29%)	5.6 months

Key: ORR=Overall Response Rate (VGPR+PR); VGPR=Very Good Partial Response; PR=Partial Response

- 1 Responses were adjudicated according to the International Myeloma Working Group criteria
- 2 Based on interim unaudited data
- 3 Five patients not evaluable for response: one death unrelated to myeloma, one non-compliance with study procedures, one withdrawal of consent before disease follow up, one death related to progressive disease (PD), one PD before C2D1
- 4 One unconfirmed VGPR

Among the patients evaluated for safety as of the data cutoff date, the most common treatment-related adverse events (AEs) were cytopenias, along with gastrointestinal and constitutional symptoms; most were manageable with dose modifications and/or standard supportive care. The most common non-hematologic treatment-related AEs were nausea (52%), fatigue (52%) and weight loss (39%). As expected, the most common treatment-related Grade 3 and 4 AEs were neutropenia (58%), thrombocytopenia (27%) and anemia (27%).

Based on these Phase 2 results, a Phase 3 study investigating the SPd combination is planned.

In parallel with the ongoing Phase 1b/2 STOMP study, Karyopharm is conducting the pivotal, randomized Phase 3 BOSTON study evaluating once-weekly selinexor in combination with the PI Velcade and dexamethasone (SVd) for the treatment of patients with multiple myeloma who have had one to three prior lines of therapy. Enrollment in the BOSTON study is complete and top-line data are expected in early 2020 contingent upon the occurrence of PFS events, the primary endpoint of the study. Data from the BOSTON study, if positive, are expected to be used to support regulatory submissions to the U.S. Food and Drug Administration and the European Medicines Agency requesting the use of selinexor in combination with Velcade and dexamethasone in patients with multiple myeloma who have received at least one prior therapy.

**New Data from Study Evaluating Selinexor in Patients with Multiple Myeloma Following CAR-T Therapy**

In this study, seven patients were identified from selinexor myeloma trials who had received an active dose of CAR-T cell therapy (>10<sup>8</sup> CAR-positive cells targeting B-cell maturation antigen) as treatment for their multiple myeloma prior to being enrolled in a trial using a selinexor-containing regimen. One patient was treated with selinexor (starting at 80 mg twice-weekly) and dexamethasone (20 mg twice weekly), one patient was treated with the regimen currently being investigated in the ongoing Phase 3 BOSTON study, a combination of selinexor (100 mg once-weekly), Velcade (1.3 mg/m<sup>2</sup> once-weekly for 4 of 5 weeks) and dexamethasone (40 mg once-weekly), and five patients were treated with a combination of selinexor (100 mg once-weekly), Kyprolis (20/56 mg/m<sup>2</sup> or 20/70 mg/m<sup>2</sup>) and dexamethasone (40 mg once weekly or 20 mg twice weekly). Patients had a median of ten prior therapeutic regimens (range: 5-15), all had high-risk cytogenetics, and six of the seven had rapidly progressing disease as indicated by the percent increase in paraprotein (17-91%) between screening and Cycle 1 Day 1 (range: 7-22 days).

The following table is a summary of the efficacy results:

**Best Responses<sup>1</sup> in Evaluable Patients<sup>2</sup>**

	N	ORR	sCR	VGPR	PR
All patients	7	6 (86%)	1 (14%)	3 (43%)	2 (29%)

Key: ORR=Overall Response Rate (CR+VGPR+PR); sCR=Stringent Complete Response

<sup>1</sup> Responses were adjudicated according to the International Myeloma Working Group criteria

<sup>2</sup> Based on interim unaudited data

Of the six patients who responded (≥PR), the duration of response ranged from 1.4 months to 7.4 months, with two patients still on therapy and responding. Adverse events were consistent with what has previously been reported with selinexor-containing regimens in heavily-pretreated patients with multiple myeloma and included nausea, fatigue, thrombocytopenia, neutropenia, and anemia.

These preliminary data suggest that selinexor-dexamethasone alone or in combination with Velcade or Kyprolis may offer a therapeutic option for patients who have exhausted other available treatments, have rapidly progressing disease, and who have progressed after CAR-T therapy.

**Details for these two ASH 2019 presentations are as follows:**

*Oral Presentation*

**Title:** Selinexor, Pomalidomide, and Dexamethasone (SPd) in Patients with Relapsed or Refractory Multiple Myeloma

**Presenter:** Christine Chen, Princess Margaret Cancer Centre

**Abstract #:** 141

**Session:** 653. Myeloma: Therapy, excluding Transplantation: New Approaches in the Treatment of Relapsed/Refractory Plasma Cell Disorders

**Date and Time:** Saturday, December 7, 2019; 9:30-11:00 AM ET

**Location:** Orange County Convention Center, Hall E1

*Poster Presentation – Company-Sponsored Studies*

**Title:** Selinexor-Containing Regimens for the Treatment of Patients with Multiple Myeloma Refractory to Chimeric Antigen Receptor T-Cell (CAR-T) Therapy

**Presenter:** Ajai Chari, Icahn School of Medicine at Mount Sinai

**Abstract #:** 1854

**Session:** 653. Myeloma: Therapy, excluding Transplantation: Poster I

**Date and Time:** Saturday, December 7, 2019; 5:30-7:30 PM ET

**Location:** Orange County Convention Center, Hall B

PDF copies of these presentations will be available [here](#) following conclusion of the presentations at the meeting.

**About XPOVIO® (selinexor)**

XPOVIO is a first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound. XPOVIO functions by selectively binding to and inhibiting the nuclear export protein exportin 1 (XPO1, also called CRM1). XPOVIO blocks the nuclear export of tumor suppressor, growth regulatory and anti-inflammatory proteins, leading to accumulation of these proteins in the nucleus and enhancing their anti-cancer activity in the cell. The forced nuclear retention of these proteins can counteract a multitude of the oncogenic pathways that, unchecked, allow cancer cells with severe DNA damage to continue to grow and divide in an unrestrained fashion. In addition to receiving accelerated FDA approval of XPOVIO in July 2019 in combination with dexamethasone for the treatment

of adult patients with relapsed refractory multiple myeloma (RRMM) 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, Karyopharm has also submitted a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) with a request for conditional approval of selinexor. Selinexor is also being studied in patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL). In 2018, Karyopharm reported positive top-line results from the Phase 2b SADAL study evaluating selinexor in patients with relapsed or refractory DLBCL after at least two prior multi-agent therapies and who are ineligible for transplantation, including high dose chemotherapy with stem cell rescue. Selinexor has received Fast Track designation from the FDA for the patient population evaluated in the SADAL study. Selinexor is also being evaluated in several other mid- and later-phase clinical trials across multiple cancer indications, including in multiple myeloma in a pivotal, randomized Phase 3 study in combination with Velcade® (bortezomib) and low-dose dexamethasone (BOSTON), as a potential backbone therapy in combination with approved therapies (STOMP), in liposarcoma (SEAL), in recurrent gliomas (KING) and in endometrial cancer (SIENDO), among others. Additional Phase 1, Phase 2 and Phase 3 studies are ongoing or currently planned, including multiple studies in combination with approved therapies in a variety of tumor types to further inform Karyopharm's clinical development priorities for selinexor. Additional clinical trial information for selinexor is available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

## IMPORTANT SAFETY INFORMATION

### Thrombocytopenia

XPOVIO can cause thrombocytopenia, leading to potentially fatal hemorrhage. Thrombocytopenia was reported as an adverse reaction in 74% of patients, and severe (Grade 3-4) thrombocytopenia occurred in 61% of patients treated with XPOVIO. The median time to onset of the first event was 22 days. Bleeding occurred in 23% of patients with thrombocytopenia, clinically significant bleeding occurred in 5% of patients with thrombocytopenia and fatal hemorrhage occurred in <1% of patients.

Monitor platelet counts at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two months of treatment. Institute platelet transfusion and/or other treatments as clinically indicated. Monitor patients for signs and symptoms of bleeding and evaluate promptly. Interrupt and/or reduce dose, or permanently discontinue based on severity of adverse reaction.

### Neutropenia

XPOVIO can cause neutropenia, potentially increasing the risk of infection. Neutropenia was reported as an adverse reaction in 34% of patients, and severe (Grade 3-4) neutropenia occurred in 21% of patients treated with XPOVIO. The median time to onset of the first event was 25 days. Febrile neutropenia was reported in 3% of patients.

Obtain neutrophil counts at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two months of treatment. Monitor patients for signs and symptoms of concomitant infection and evaluate promptly. Consider supportive measures including antimicrobials for signs of infection and use of growth factors (e.g., G-CSF). Interrupt and/or reduce dose, or permanently discontinue based on severity of adverse reaction.

### **Gastrointestinal Toxicity**

Gastrointestinal toxicities occurred in patients treated with XPOVIO.

#### **Nausea/Vomiting**

Nausea was reported as an adverse reaction in 72% of patients, and Grade 3 nausea occurred in 9% of patients treated with XPOVIO. The median time to onset of the first nausea event was 3 days.

Vomiting was reported in 41% of patients, and Grade 3 vomiting occurred in 4% of patients treated with XPOVIO. The median time to onset of the first vomiting event was 5 days.

Provide prophylactic 5-HT<sub>3</sub> antagonists and/or other anti-nausea agents, prior to and during treatment with XPOVIO. Manage nausea/vomiting by dose interruption, reduction, and/or discontinuation. Administer intravenous fluids and replace electrolytes to prevent dehydration in patients at risk. Use additional anti-nausea medications as clinically indicated.

#### **Diarrhea**

Diarrhea was reported as an adverse reaction in 44% of patients, and Grade 3 diarrhea occurred in 6% of patients treated with XPOVIO. The median time to onset of diarrhea was 15 days.

Manage diarrhea by dose modifications and/or standard anti-diarrheal agents; administer intravenous fluids to prevent dehydration in patients at risk.

#### **Anorexia/Weight Loss**

Anorexia was reported as an adverse reaction in 53% of patients, and Grade 3 anorexia occurred in 5% of patients treated with XPOVIO. The median time to onset of anorexia was 8 days.

Weight loss was reported as an adverse reaction in 47% of patients, and Grade 3 weight loss occurred in 1% of patients treated with XPOVIO. The median time to onset of weight loss was 15 days.

Monitor patient weight at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two months of treatment. Manage anorexia and weight loss with dose modifications, appetite stimulants, and nutritional support.

#### **Hyponatremia**

XPOVIO can cause hyponatremia; 39% of patients treated with XPOVIO experienced hyponatremia, 22% of patients experienced Grade 3 or 4 hyponatremia. The median time to onset of the first event was 8 days.

Monitor sodium level at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two months of treatment. Correct sodium levels for concurrent hyperglycemia (serum glucose >150 mg/dL) and high serum paraprotein levels. Treat hyponatremia per clinical guidelines (intravenous saline and/or salt tablets), including dietary review. Interrupt and/or reduce dose, or permanently discontinue based on severity of adverse reaction.

**Infections**

In patients receiving XPOVIO, 52% of patients experienced any grade of infection. Upper respiratory tract infection of any grade occurred in 21%, pneumonia in 13%, and sepsis in 6% of patients. Grade  $\geq 3$  infections were reported in 25% of patients, and deaths resulting from an infection occurred in 4% of patients. The most commonly reported Grade  $\geq 3$  infections were pneumonia in 9% of patients, followed by sepsis in 6%. The median time to onset was 54 days for pneumonia and 42 days for sepsis. Most infections were not associated with neutropenia and were caused by non-opportunistic organisms.

**Neurological Toxicity**

Neurological toxicities occurred in patients treated with XPOVIO.

Neurological adverse reactions including dizziness, syncope, depressed level of consciousness, and mental status changes (including delirium and confusional state) occurred in 30% of patients, and severe events (Grade 3-4) occurred in 9% of patients treated with XPOVIO. Median time to the first event was 15 days.

Optimize hydration status, hemoglobin level, and concomitant medications to avoid exacerbating dizziness or mental status changes.

**Embryo-Fetal Toxicity**

Based on data from animal studies and its mechanism of action, XPOVIO can cause fetal harm when administered to a pregnant woman. Selinexor administration to pregnant animals during organogenesis resulted in structural abnormalities and alterations to growth at exposures below those occurring clinically at the recommended dose.

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with a female partner of reproductive potential to use effective contraception during treatment with XPOVIO and for 1 week after the last dose.

**ADVERSE REACTIONS**

The most common adverse reactions (incidence  $\geq 20\%$ ) are thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea, and upper respiratory tract infection.

The treatment discontinuation rate due to adverse reactions was 27%; 53% of patients had a reduction in the XPOVIO dose, and 65.3% had the dose of XPOVIO interrupted. The most frequent adverse reactions requiring permanent discontinuation in 4% or greater of patients who received XPOVIO included fatigue, nausea, and thrombocytopenia. The rate of fatal adverse reactions was 8.9%.

**Please see XPOVIO Full Prescribing Information available at [www.XPOVIO.com](http://www.XPOVIO.com).**

**About Karyopharm Therapeutics**

Karyopharm Therapeutics Inc. (Nasdaq: KPTI) is an oncology-focused pharmaceutical company 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. Karyopharm's SINE compounds function by binding with and inhibiting the nuclear export protein XPO1 (or CRM1). Karyopharm's lead compound, XPOVIO® (selinexor), received accelerated approval from the FDA in July 2019 in combination with dexamethasone as a

treatment for patients with heavily pretreated multiple myeloma. A Marketing Authorization Application for selinexor is also currently under review by the European Medicines Agency (EMA). In addition to single-agent and combination activity against a variety of human cancers, SINE compounds have also shown biological activity in models of neurodegeneration, inflammation, autoimmune disease, certain viruses and wound-healing. Karyopharm has several investigational programs in clinical or preclinical development. For more information, please visit [www.karyopharm.com](http://www.karyopharm.com).

### Forward-Looking Statements

This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding Karyopharm's expectations relating to XPOVIO for the treatment of patients with heavily pretreated multiple myeloma, commercialization of XPOVIO or any of its drug candidates, submissions to, and the review and potential approval of selinexor by, regulatory authorities, including the anticipated availability of data to support such submissions, timing of such submissions and actions by regulatory authorities and the potential availability of accelerated approval pathways, and the therapeutic potential of and potential clinical development plans for Karyopharm's drug candidates, especially selinexor. Such statements are subject to numerous important factors, risks and uncertainties, many of which are beyond Karyopharm's control, that may cause actual events or results to differ materially from Karyopharm's current expectations. For example, there can be no guarantee that Karyopharm will successfully commercialize XPOVIO; that regulators will agree that selinexor qualifies for conditional approval in the E.U. as a result of data from the STORM study or confirmatory approval in the U.S. or EU based on the BOSTON study in patients with relapsed or refractory multiple myeloma, or that any of Karyopharm's drug candidates, including selinexor, will successfully complete necessary clinical development phases or that development of any of Karyopharm's drug candidates will continue. Further, there can be no guarantee that any positive developments in the development or commercialization of Karyopharm's drug candidate portfolio will result in stock price appreciation. Management's expectations and, therefore, any forward-looking statements in this press release could also be affected by risks and uncertainties relating to a number of other factors, including the following: adoption of XPOVIO in the commercial marketplace, the timing and costs involved in commercializing XPOVIO or any of Karyopharm's drug candidates that receive regulatory approval; the ability to retain regulatory approval of XPOVIO or any of Karyopharm's drug candidates that receive regulatory approval; Karyopharm's results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; the content and timing of decisions made by the U.S. Food and Drug Administration and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies, including with respect to the need for additional clinical studies; the ability of Karyopharm or its third party collaborators or successors in interest to fully perform their respective obligations under the applicable agreement and the potential future financial implications of such agreement; Karyopharm's ability to obtain and maintain requisite regulatory approvals and to enroll patients in its clinical trials; unplanned cash requirements and expenditures; development of drug candidates by Karyopharm's competitors for diseases in which Karyopharm is currently developing its drug candidates; and Karyopharm's ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing. These and other risks are described under the caption "Risk Factors" in Karyopharm's Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, which was filed with the Securities and Exchange Commission (SEC) on November 4, 2019, and in other filings that Karyopharm may make with the SEC in the future. Any forward-looking statements contained in this press release speak only as of the date hereof, and, except as required by law, Karyopharm expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.



Velcade® is a registered trademark of Takeda Pharmaceutical Company Limited  
Revlimid® and Pomalyst® are registered trademarks of Celgene Corporation  
Kyprolis® is a registered trademark of Onyx Pharmaceuticals, Inc.

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**Karyopharm Presents XPOVIO® (Selinexor) and Eltanexor Data at the American Society of Hematology 2019 Annual Meeting**

- *Once-Weekly Oral Selinexor in Combination with Weekly Kyprolis® and Low Dose Dexamethasone Demonstrates 71% Overall Response Rate, Including a Complete Response Rate of 21%, in Patients with Heavily Pretreated, Kyprolis-Naïve Multiple Myeloma* —
- *All Oral Regimen of Once-Weekly Selinexor with Revlimid® and Low Dose Dexamethasone Achieves High Response Rates in Patients with Newly Diagnosed Multiple Myeloma* —
- *STORM Study Patients Treated with Selinexor Achieved Survival Advantage Over Matched Patients from the MAMMOTH Study Who Were Treated with Other Anti-Myeloma Agents* —
- *Single-Agent Oral Eltanexor Shows Encouraging Activity in Elderly Patients with Higher-Risk Myelodysplastic Syndrome* —

**NEWTON, Mass.** – December 8, 2019 – Karyopharm Therapeutics Inc. (Nasdaq:KPTI), an oncology-focused pharmaceutical company, today announced that four posters relating to XPOVIO® (selinexor), the Company’s first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound, and eltanexor, its next generation SINE compound, will be presented at the American Society of Hematology (ASH) 2019 Annual Meeting taking place December 7-10, 2019 in Orlando. The four posters include: updated data from the Kyprolis® (carfilzomib) arm of the Phase 1b/2 STOMP study evaluating selinexor in combination with backbone therapies in patients with relapsed or refractory multiple myeloma; new data from the Revlimid® (lenalidomide) plus selinexor arm of the STOMP study evaluating this combination in patients with newly diagnosed multiple myeloma; encore data highlighting the previously disclosed comparison of patients in the STORM study, Karyopharm’s Phase 2b study evaluating XPOVIO® in patients with heavily pretreated, triple class refractory multiple myeloma, to matched patients from the MAMMOTH study; and new Phase 1/2 data evaluating eltanexor in patients with higher-risk myelodysplastic syndrome (MDS).

“Efficacy data from our ongoing STOMP study investigating selinexor in combination with standard of care anti-myeloma agents continue to demonstrate a strong rationale for selinexor’s potential expanded role in the future multiple myeloma treatment paradigm,” said Sharon Shacham, PhD, MBA, Founder, President and Chief Scientific Officer of Karyopharm. “The Kyprolis arm of the STOMP study continues to show clear signs of clinical activity, including a complete response rate of 21%, in patients with heavily pretreated Kyprolis-naïve multiple myeloma. Additionally, preliminary data from the Revlimid arm of the Phase 1b/2 STOMP study show early but encouraging clinical activity, including in one patient who achieved a complete response, in patients with multiple myeloma in the front-line setting. And finally, we are pleased to be presenting new data from the eltanexor program showing impressive early activity, including a high rate of complete responses in elderly patients with higher-risk MDS.”

**Updated Data from Phase 1b/2 STOMP Study Evaluating Selinexor in Combination with Kyprolis and Low-dose Dexamethasone (SKd) in Patient with Relapsed or Refractory Multiple Myeloma**

In this arm of the Phase 1b/2 STOMP study, oral selinexor (dosed once-weekly) is being evaluated in combination with Kyprolis (56mg/m<sup>2</sup> or 70mg/m<sup>2</sup> once weekly) and low dose dexamethasone (orally, 40mg once weekly or 20mg twice weekly) in patients with relapsed refractory multiple myeloma who have received at least two prior therapies, which can include previous treatment with a proteasome inhibitor, one or more immunomodulatory drugs (e.g., Revlimid or Pomalyst) or Darzalex. The median number of prior treatments was four (range: 2-8). The following table is a summary of the efficacy results:

**Best Responses<sup>1</sup> in Evaluable SKd Patients as of 1-Oct-2019<sup>2</sup>**

Category	N	ORR	CR	VGPR	PR
All (Kyprolis-naïve)	14	10 (71%)	3 (21%)	7 (50%)	—

Key: ORR=Overall Response Rate (CR+VGPR+PR); CR=Complete Response; VGPR=Very Good Partial Response; PR=Partial Response

<sup>1</sup> Responses were adjudicated according to the International Myeloma Working Group criteria

<sup>2</sup> Based on interim unaudited data

All patients had reductions in M-protein from baseline, with 71% of patients experiencing a reduction of ≥90%. Median progression-free survival (PFS) has not yet been reached.

Among the patients evaluated for safety as of the data cutoff date, the most common treatment-related adverse events (AEs) were cytopenias, along with gastrointestinal and constitutional symptoms; most were manageable with dose modifications and/or standard supportive care. The most common non-hematologic treatment-related AEs were nausea (71%), fatigue (43%), anorexia (36%), vomiting (36%) and weight loss (36%), and were mostly Grade 1 and 2 events. As expected, the most common treatment-related Grade ≥3 AEs were hematologic AEs and included thrombocytopenia (64%), anemia (14%) and leukopenia (14%). The recommended Phase 2 dose (RP2D) was identified as selinexor 80mg and Kyprolis 56mg/m<sup>2</sup> and enrollment continues using this regimen.

**New Data from Phase 1b/2 STOMP Study Evaluating the All Oral Combination of Selinexor with Revlimid and Low-dose Dexamethasone (SRd) in Patients with Newly Diagnosed Multiple Myeloma**

In this all oral arm of the Phase 1b/2 STOMP study in patients with newly diagnosed multiple myeloma, selinexor (60mg once-weekly) is being combined with Revlimid (25mg orally, once daily) and low dose dexamethasone (orally, 40mg once weekly or 20mg twice weekly). The following table is a summary of the efficacy results:

**Best Responses<sup>1</sup> in Evaluable SRd Patients as of 1-Oct-2019<sup>2</sup>**

Category	N <sup>3</sup>	ORR	CR	VGPR <sup>4</sup>	PR
All	7	6 (86%)	1 (14%)	4 (57%)	1 (14%)

Key: ORR=Overall Response Rate (CR+VGPR+PR)

<sup>1</sup> Responses were adjudicated according to the International Myeloma Working Group criteria

<sup>2</sup> Based on interim unaudited data

<sup>3</sup> One patient was not evaluable for response due to withdrawn consent prior to disease follow-up

<sup>4</sup> One VGPR was confirmed on Oct 10, 2019 (after data cut); two VGPR are unconfirmed

The data are early and the median PFS was not reached. Among the patients evaluable for safety, the most common treatment-related AEs were cytopenias, along with gastrointestinal and constitutional symptoms; most were manageable with dose modifications and/or standard supportive care. The most common non-hematologic treatment-related AEs were diarrhea (63%), weight loss (63%), nausea (50%), constipation (38%), fatigue (38%), hypokalemia (38%) and insomnia (38%) and were mostly Grade 1/2. The most common Grade ≥3 AEs were neutropenia (75%), anemia (50%) and thrombocytopenia (25%). Amongst the five patients evaluable for dose limiting toxicities (DLTs), there were no DLTs observed.

**Comparison of Overall Survival Rates Between the Phase 2b STORM Study and the MAMMOTH Study**

Another key presentation at ASH 2019 highlights encore data comparing the overall survival (OS) rate from the retrospective MAMMOTH study (Leukemia, 2019). The MAMMOTH study evaluated outcomes of patients with relapsed or refractory multiple myeloma (RRMM) treated at major academic medical centers. This ASH presentation highlighted results from a comparison of outcomes from patients with RRMM after their disease became refractory to CD38 monoclonal antibodies with a matched cohort of patients from Karyopharm’s Phase 2b STORM study, which served as the basis for the XPOVIO accelerated approval. Thus, patients in STORM who received selinexor and dexamethasone as first line of therapy after their disease became triple class refractory (n=64) were compared with matched patients receiving currently available therapies from the MAMMOTH cohort (n=128), showed an unadjusted hazard ratio (HR) for death of 0.64 (p=0.043), while an adjusted analysis, which takes into consideration differences in baseline characteristics between the two groups, showed a HR of 0.55 (p=0.009). The median OS of patients in STORM was 10.4 months and in MAMMOTH was 6.9 months. These results are consistent with previous presented results of STORM patients versus those from the Flatiron Health Analytics Database (FHAD) from patients with RRMM treated primarily in the community setting (Richardson, *et al.* ASCO 2019). In that analysis, the median OS of patients in STORM was 10.4 months and in FHAD was 5.8 months (p=0.036).

**Updated Phase 1/2 Clinical Data for Oral Eltanexor in Elderly Patients with Higher-Risk MDS**

This Phase 1/2 study is evaluating the safety, tolerability and anti-tumor activity of single-agent oral eltanexor (10mg or 20mg once-daily for 5 days per week) in elderly patients with higher-risk MDS. All patients were refractory to hypomethylating agents. The following table is a summary of the efficacy results:

**Best Responses<sup>1</sup> in Eltanexor Patients<sup>2</sup>**

Category	N	ORR	mCR	SD
All patients	20	7 (35%)	7 (35%)	5 (25%)

Key: ORR=Overall Response Rate (mCR+HI [not observed]); mCR=Complete Response without marrow recovery; HI=Hematologic Improvement; SD=Stable Disease

- <sup>1</sup> Responses assessments were made by the treating physician according to the 2006 International Working Group (IWG) Response Criteria for MDS
- <sup>2</sup> Based on interim unaudited data

Median overall survival was 10.6 months. The most common treatment-related AEs were hematologic, gastrointestinal and constitutional. The most common non-hematologic treatment-related AEs were nausea (45%), decreased appetite (40%), fatigue (35%), diarrhea (35%) and dysgeusia (25%); the vast majority were Grade 1 or 2. The most common Grade ≥3 AEs were anemia (30%), neutropenia (25%), thrombocytopenia (20%) and leukopenia (15%). AEs were dose-dependent and managed with supportive care and dose modification. This Phase 1/2 study remains ongoing.

**Other Key Selinexor Presentations**

An additional investigator-sponsored study, which will be presented on Monday, December 9, 2019, highlights data from a Phase 1 trial investigating the combination of selinexor and ibrutinib in 33 heavily pretreated, high-risk patients with chronic lymphocytic leukemia or non-Hodgkin lymphoma. This combination was tolerable and demonstrated encouraging efficacy in this high-unmet need patient population warranting additional future clinical investigation.

**Details for these ASH 2019 presentations are as follows:***Poster Presentations – Company-Sponsored Studies***Title:** Safety and Efficacy of the Combination of Selinexor, Lenalidomide and Dexamethasone (SRd) in Patients with Newly Diagnosed Multiple Myeloma**Presenter:** Darrell White, Dalhousie University**Abstract #:** 3165**Session:** 653. Myeloma: Therapy, excluding Transplantation: Poster II**Date and Time:** Sunday, December 8, 2019; 6:00-8:00 PM ET**Location:** Orange County Convention Center, Hall B**Title:** A Phase 1b/2 Study of Selinexor, Carfilzomib, and Dexamethasone (SKd) in Relapsed/ Refractory Multiple Myeloma (RRMM)**Presenter:** Cristina Gasparetto, Duke University Medical Center**Abstract #:** 3157**Session:** 653. Myeloma: Therapy, excluding Transplantation: Poster II**Date and Time:** Sunday, December 8, 2019; 6:00-8:00 PM ET**Location:** Orange County Convention Center, Hall B**Title:** Overall Survival of Triple Class Refractory, Penta-Exposed Multiple Myeloma (MM) Patients Treated with Selinexor Plus Dexamethasone or Conventional Care: A Combined Analysis of the STORM and Mammoth Studies**Presenter:** Luciano Costa, University of Alabama at Birmingham**Abstract #:** 3125**Session:** 653. Myeloma: Therapy, excluding Transplantation: Poster II**Date and Time:** Date: Sunday, December 8, 2019; 6:00 PM - 8:00 PM ET**Location:** Orange County Convention Center, Hall B**Title:** Eltanexor (KPT-8602), a Second-Generation Selective Inhibitor of Nuclear Export (SINE) Compound, in Patients with Higher-Risk Myelodysplastic Syndrome**Presenter:** Sangmin Lee, Weill Cornell School of Medicine**Abstract #:** 2997**Session:** 637. Myelodysplastic Syndromes—Clinical Studies: Poster II**Date and Time:** Sunday, December 8, 2019; 6:00-8:00 PM ET**Location:** Orange County Convention Center, Hall B*Poster Presentations – Investigator-Sponsored Studies***Title:** Selinexor Combined with Ibrutinib Demonstrates Tolerability and Efficacy in Advanced B-Cell Malignancies: A Phase I Study**Presenter:** Deborah Stephens, Huntsman Cancer Institute, University of Utah**Abstract #:** 4310**Session:** 642. CLL: Therapy, excluding Transplantation: Poster III**Date and Time:** Monday, December 9, 2019; 6:00-8:00 PM ET**Location:** Orange County Convention Center, Hall BPDF copies of these presentations will be available [here](#) following conclusion of the presentations at the meeting.

### About XPOVIO® (selinexor)

XPOVIO is a first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound. XPOVIO functions by selectively binding to and inhibiting the nuclear export protein exportin 1 (XPO1, also called CRM1). XPOVIO blocks the nuclear export of tumor suppressor, growth regulatory and anti-inflammatory proteins, leading to accumulation of these proteins in the nucleus and enhancing their anti-cancer activity in the cell. The forced nuclear retention of these proteins can counteract a multitude of the oncogenic pathways that, unchecked, allow cancer cells with severe DNA damage to continue to grow and divide in an unrestrained fashion. In addition to receiving accelerated U.S. Food and Drug Administration (FDA) approval of XPOVIO in July 2019 in combination with dexamethasone for the treatment of adult patients with relapsed refractory multiple myeloma (RRMM) 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, Karyopharm has also submitted a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) with a request for conditional approval of selinexor. Selinexor is also being studied in patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL). In 2018, Karyopharm reported positive top-line results from the Phase 2b SADAL study evaluating selinexor in patients with relapsed or refractory DLBCL after at least two prior multi-agent therapies and who are ineligible for transplantation, including high dose chemotherapy with stem cell rescue. Selinexor has received Fast Track designation from the FDA for the patient population evaluated in the SADAL study. Selinexor is also being evaluated in several other mid-and later-phase clinical trials across multiple cancer indications, including in multiple myeloma in a pivotal, randomized Phase 3 study in combination with Velcade® (bortezomib) and low-dose dexamethasone (BOSTON), as a potential backbone therapy in combination with approved therapies (STOMP), in liposarcoma (SEAL), in recurrent gliomas (KING) and in endometrial cancer (SIENDO), among others. Additional Phase 1, Phase 2 and Phase 3 studies are ongoing or currently planned, including multiple studies in combination with approved therapies in a variety of tumor types to further inform Karyopharm's clinical development priorities for selinexor. Additional clinical trial information for selinexor is available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

### IMPORTANT SAFETY INFORMATION

#### Thrombocytopenia

XPOVIO can cause thrombocytopenia, leading to potentially fatal hemorrhage. Thrombocytopenia was reported as an adverse reaction in 74% of patients, and severe (Grade 3-4) thrombocytopenia occurred in 61% of patients treated with XPOVIO. The median time to onset of the first event was 22 days. Bleeding occurred in 23% of patients with thrombocytopenia, clinically significant bleeding occurred in 5% of patients with thrombocytopenia and fatal hemorrhage occurred in <1% of patients.

Monitor platelet counts at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two months of treatment. Institute platelet transfusion and/or other treatments as clinically indicated. Monitor patients for signs and symptoms of bleeding and evaluate promptly. Interrupt and/or reduce dose, or permanently discontinue based on severity of adverse reaction.

#### Neutropenia

XPOVIO can cause neutropenia, potentially increasing the risk of infection. Neutropenia was reported as an adverse reaction in 34% of patients, and severe (Grade 3-4) neutropenia occurred in 21% of patients treated with XPOVIO. The median time to onset of the first event was 25 days. Febrile neutropenia was reported in 3% of patients.

Obtain neutrophil counts at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two months of treatment. Monitor patients for signs and symptoms of concomitant infection and evaluate promptly. Consider supportive measures including antimicrobials for signs of infection and use of growth factors (e.g., G-CSF). Interrupt and/or reduce dose, or permanently discontinue based on severity of adverse reaction.

#### **Gastrointestinal Toxicity**

Gastrointestinal toxicities occurred in patients treated with XPOVIO.

#### **Nausea/Vomiting**

Nausea was reported as an adverse reaction in 72% of patients, and Grade 3 nausea occurred in 9% of patients treated with XPOVIO. The median time to onset of the first nausea event was 3 days.

Vomiting was reported in 41% of patients, and Grade 3 vomiting occurred in 4% of patients treated with XPOVIO. The median time to onset of the first vomiting event was 5 days.

Provide prophylactic 5-HT<sub>3</sub> antagonists and/or other anti-nausea agents, prior to and during treatment with XPOVIO. Manage nausea/vomiting by dose interruption, reduction, and/or discontinuation. Administer intravenous fluids and replace electrolytes to prevent dehydration in patients at risk. Use additional anti-nausea medications as clinically indicated.

#### **Diarrhea**

Diarrhea was reported as an adverse reaction in 44% of patients, and Grade 3 diarrhea occurred in 6% of patients treated with XPOVIO. The median time to onset of diarrhea was 15 days.

Manage diarrhea by dose modifications and/or standard anti-diarrheal agents; administer intravenous fluids to prevent dehydration in patients at risk.

#### **Anorexia/Weight Loss**

Anorexia was reported as an adverse reaction in 53% of patients, and Grade 3 anorexia occurred in 5% of patients treated with XPOVIO. The median time to onset of anorexia was 8 days.

Weight loss was reported as an adverse reaction in 47% of patients, and Grade 3 weight loss occurred in 1% of patients treated with XPOVIO. The median time to onset of weight loss was 15 days.

Monitor patient weight at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two months of treatment. Manage anorexia and weight loss with dose modifications, appetite stimulants, and nutritional support.

#### **Hyponatremia**

XPOVIO can cause hyponatremia; 39% of patients treated with XPOVIO experienced hyponatremia, 22% of patients experienced Grade 3 or 4 hyponatremia. The median time to onset of the first event was 8 days.

Monitor sodium level at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two months of treatment. Correct sodium levels for concurrent hyperglycemia (serum glucose >150 mg/dL) and high serum paraprotein levels. Treat hyponatremia per clinical guidelines (intravenous saline and/or salt tablets), including dietary review. Interrupt and/or reduce dose, or permanently discontinue based on severity of adverse reaction.

### **Infections**

In patients receiving XPOVIO, 52% of patients experienced any grade of infection. Upper respiratory tract infection of any grade occurred in 21%, pneumonia in 13%, and sepsis in 6% of patients. Grade  $\geq 3$  infections were reported in 25% of patients, and deaths resulting from an infection occurred in 4% of patients. The most commonly reported Grade  $\geq 3$  infections were pneumonia in 9% of patients, followed by sepsis in 6%. The median time to onset was 54 days for pneumonia and 42 days for sepsis. Most infections were not associated with neutropenia and were caused by non-opportunistic organisms.

### **Neurological Toxicity**

Neurological toxicities occurred in patients treated with XPOVIO.

Neurological adverse reactions including dizziness, syncope, depressed level of consciousness, and mental status changes (including delirium and confusional state) occurred in 30% of patients, and severe events (Grade 3-4) occurred in 9% of patients treated with XPOVIO. Median time to the first event was 15 days.

Optimize hydration status, hemoglobin level, and concomitant medications to avoid exacerbating dizziness or mental status changes.

### **Embryo-Fetal Toxicity**

Based on data from animal studies and its mechanism of action, XPOVIO can cause fetal harm when administered to a pregnant woman. Selinexor administration to pregnant animals during organogenesis resulted in structural abnormalities and alterations to growth at exposures below those occurring clinically at the recommended dose.

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with a female partner of reproductive potential to use effective contraception during treatment with XPOVIO and for 1 week after the last dose.

### **ADVERSE REACTIONS**

The most common adverse reactions (incidence  $\geq 20\%$ ) are thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea, and upper respiratory tract infection.

The treatment discontinuation rate due to adverse reactions was 27%; 53% of patients had a reduction in the XPOVIO dose, and 65.3% had the dose of XPOVIO interrupted. The most frequent adverse reactions requiring permanent discontinuation in 4% or greater of patients who received XPOVIO included fatigue, nausea, and thrombocytopenia. The rate of fatal adverse reactions was 8.9%.

**Please see XPOVIO Full Prescribing Information available at [www.XPOVIO.com](http://www.XPOVIO.com).**

### About Eltanexor (KPT-8602)

Eltanexor (KPT-8602) is a second generation oral SINE compound, which is currently being investigated in clinical trials. Eltanexor functions by binding to and inhibiting the nuclear export protein XPO1 (also called CRM1), leading to the accumulation of tumor suppressor proteins in the cell nucleus. Eltanexor has demonstrated minimal brain penetration in animals, which has been associated with reduced toxicities in preclinical studies while maintaining potent anti-tumor effects.

### About Karyopharm Therapeutics

Karyopharm Therapeutics Inc. (Nasdaq: KPTI) is an oncology-focused pharmaceutical company 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. Karyopharm's SINE compounds function by binding with and inhibiting the nuclear export protein XPO1 (or CRM1). Karyopharm's lead compound, XPOVIO® (selinexor), received accelerated approval from the FDA in July 2019 in combination with dexamethasone as a treatment for patients with heavily pretreated multiple myeloma. A Marketing Authorization Application for selinexor is also currently under review by the European Medicines Agency (EMA). In addition to single-agent and combination activity against a variety of human cancers, SINE compounds have also shown biological activity in models of neurodegeneration, inflammation, autoimmune disease, certain viruses and wound-healing. Karyopharm has several investigational programs in clinical or preclinical development. For more information, please visit [www.karyopharm.com](http://www.karyopharm.com).

### Forward-Looking Statements

This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding Karyopharm's expectations relating to XPOVIO for the treatment of patients with heavily pretreated multiple myeloma, commercialization of XPOVIO or any of its drug candidates, submissions to, and the review and potential approval of selinexor by, regulatory authorities, including the anticipated availability of data to support such submissions, timing of such submissions and actions by regulatory authorities and the potential availability of accelerated approval pathways, and the therapeutic potential of and potential clinical development plans for Karyopharm's drug candidates, especially selinexor. Such statements are subject to numerous important factors, risks and uncertainties, many of which are beyond Karyopharm's control, that may cause actual events or results to differ materially from Karyopharm's current expectations. For example, there can be no guarantee that Karyopharm will successfully commercialize XPOVIO; that regulators will agree that selinexor qualifies for conditional approval in the E.U. as a result of data from the STORM study or confirmatory approval in the U.S. or EU based on the BOSTON study in patients with relapsed or refractory multiple myeloma, or that any of Karyopharm's drug candidates, including selinexor, will successfully complete necessary clinical development phases or that development of any of Karyopharm's drug candidates will continue. Further, there can be no guarantee that any positive developments in the development or commercialization of Karyopharm's drug candidate portfolio will result in stock price appreciation. Management's expectations and, therefore, any forward-looking statements in this press release could also be affected by risks and uncertainties relating to a number of other factors, including the following: adoption of XPOVIO in the commercial marketplace, the timing and costs involved in commercializing XPOVIO or any of Karyopharm's drug candidates that receive regulatory approval; the ability to retain regulatory approval of XPOVIO or any of Karyopharm's drug candidates that receive regulatory approval; Karyopharm's results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; the content and timing of decisions made by the U.S. Food and Drug Administration and other

regulatory authorities, investigational review boards at clinical trial sites and publication review bodies, including with respect to the need for additional clinical studies; the ability of Karyopharm or its third party collaborators or successors in interest to fully perform their respective obligations under the applicable agreement and the potential future financial implications of such agreement; Karyopharm's ability to obtain and maintain requisite regulatory approvals and to enroll patients in its clinical trials; unplanned cash requirements and expenditures; development of drug candidates by Karyopharm's competitors for diseases in which Karyopharm is currently developing its drug candidates; and Karyopharm's ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing. These and other risks are described under the caption "Risk Factors" in Karyopharm's Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, which was filed with the Securities and Exchange Commission (SEC) on November 4, 2019, and in other filings that Karyopharm may make with the SEC in the future. Any forward-looking statements contained in this press release speak only as of the date hereof, and, except as required by law, Karyopharm expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

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