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**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 1, 2018**

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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))

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 1, 2018, Karyopharm Therapeutics Inc. (the “Company”) issued a press release announcing the presentation of topline results from the Phase 2b SADAL study at the American Society of Hematology 2018 Annual Meeting (the “ASH Annual Meeting”).

On December 3, 2018, the Company issued a press release announcing the presentation of updated clinical data from the Phase 2b STORM study and from two treatment arms of the Phase 1b/2 STOMP study at the ASH Annual Meeting.

Copies of the press releases are filed as Exhibit 99.1 and Exhibit 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 1, 2018](#)

99.2 [Press release issued by Karyopharm Therapeutics Inc. on December 3, 2018](#)

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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.

KARYOPHARM THERAPEUTICS INC.

Date: December 3, 2018

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



## Targeting Disease at the Nuclear Pore

### Karyopharm Reports Positive Top-Line Phase 2b SADAL Data for Selinexor in Patients with Diffuse Large B-Cell Lymphoma at the American Society of Hematology 2018 Annual Meeting

*– 29.6% Overall Response Rate Including 9.6% Complete Response Rate –*

*– Amongst the Patients with Complete or Partial Response, Median Duration of Response was 9.2 Months and Median Overall Survival was 29.7 months –*

*– Company Plans to Submit New Drug Application to the FDA in the First Half of 2019 –*

**NEWTON, Mass.** – December 1, 2018 – Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today reported positive top-line results from the Phase 2b SADAL (**S**elinexor **A**gainst **D**iffuse **A**ggressive **L**ymphoma) study evaluating selinexor, the Company's first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound, in patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after at least two prior multi-agent therapies and who are ineligible for transplantation, including high dose chemotherapy with stem cell rescue. The data were highlighted in a poster presentation at the American Society of Hematology (ASH) 2018 Annual Meeting in San Diego. For the SADAL study's primary endpoint, single-agent selinexor achieved a 29.6% overall response rate (ORR), which included a 9.6% complete response (CR) rate in patients with heavily pretreated relapsed or refractory DLBCL. Key secondary endpoints included a median duration of response (DOR, in the responding patients) of 9.2 months and median overall survival (OS, across the entire study) of 9.1 months.

Selinexor recently received Fast Track designation from the FDA for the patient population evaluated in the SADAL study. Karyopharm plans to submit a New Drug Application (NDA) to the FDA during the first half of 2019, with a request for accelerated approval for oral single-agent selinexor as a new treatment for patients with relapsed or refractory DLBCL.

#### Top-Line Phase 2b SADAL Results

Based on the modified intention-to-treat analysis from the first 115 of 127 patients (median of 2 prior treatment regimens with a range 1-6), as adjudicated by an independent central radiological committee, 34 patients responded (11 patients with a CR and 23 patients with a PR) for an ORR of 29.6%. An additional 8 patients experienced stable disease (SD) for a disease control rate of 36.5%. The median DOR across responding patients was 9.2 months and responses tended to occur rapidly. Patients with a CR had a median DOR of 23.0 months and patients with a PR had a median DOR of 7.8 months. As of the data cutoff date of November 15, 2018, 7 patients who achieved a CR remained on treatment. In addition, 12 patients remain on treatment, but as of November 15<sup>th</sup>, had not reached their first response assessment and are not included in the top-line efficacy analyses.

Among the patients evaluated for safety as of the data cutoff date, the most common treatment-related adverse events (AEs) were gastrointestinal and constitutional symptoms, along with cytopenias; most manageable with dose modifications and/or supportive care. The most common non-hematologic AEs were nausea (50.0%), fatigue (35.9%), and anorexia (32.0%) and mostly Grade 1 and 2 events. As expected, the most common Grade 3 and 4 AEs were thrombocytopenia (35.2%), neutropenia (20.3%), and anemia (10.9%) and were generally not associated with clinical sequelae. No significant major organ toxicities were observed, and bleeding and infection rates were low.

The median OS was 9.1 months for all patients in the study. As of the data cutoff date, median survival for the patients with a CR or PR was 29.7 months. The median survival for patients with best response of progressive disease or who were not evaluable for response was 3.2 months.

Selinexor showed robust, single-agent activity in patients with either GCB or non-GCB subtypes of DLBCL: of the 53 patients with the GCB-subtype, 18 responded (5 patients with a CR and 13 patients with a PR) for an ORR of 34.0%. Of the 57 patients with the non-GCB subtype, 12 responded (6 patients with a CR and 6 patients with a PR) for an ORR of 21.1%. In addition, there were 5 patients enrolled whose subtype was unclassified and 4 of these patients achieved a PR.

“The SADAL data presented at ASH this year demonstrate that oral selinexor, when administered as a single-agent, is clinically active and capable of producing durable responses associated with prolonged overall survival,” said Marie Maerevoet, MD, Institute Jules Bordet, “The 60mg twice weekly oral dose continues to be well tolerated with a low incidence of Grade 3 or greater adverse events, which were often manageable with dose modifications and supportive care. We are highly encouraged by the results of this single agent study in patients with heavily pretreated DLBCL who have limited available treatment options.”

Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm, said, “In addition to the compelling efficacy and safety data observed with single agent oral selinexor, we were especially pleased to see strong response rates in patients with both the GCB and non-GCB subtypes. This is especially important because the prognosis in patients with refractory disease and the GCB-subtype is particularly poor. We believe that if selinexor is ultimately approved for use in patients with DLBCL, it will provide a meaningful therapeutic option for patients battling refractory disease regardless of DLBCL subtype. We look forward to submitting these data to the FDA during the first half of 2019 as part of a New Drug Application, with a request for accelerated approval.”

#### **Details for the Poster Presentation at ASH 2018:**

**Title:** Single Agent Oral Selinexor Demonstrates Deep and Durable Responses in Relapsed/Refractory Diffuse Large B-Cell Lymphoma (DLBCL) in Both GCB and Non-GCB Subtypes: The Phase 2b SADAL Study

**Presenter:** Marie Maerevoet, Institute Jules Bordet, Brussels, Belgium

**Abstract Number/Publication ID:** 1677

**Session:** 626. Aggressive Lymphoma (Diffuse Large B-Cell and Other Aggressive B-Cell Non-Hodgkin Lymphomas)—Results from Prospective Clinical Trials: Poster I

**Date and Time:** Saturday, December 1, 2018; 6:15-8:15 PM PT

**Location:** San Diego Convention Center, Hall GH

#### **About Selinexor**

Selinexor is a first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound. Selinexor functions by binding with and inhibiting the nuclear export protein XPO1 (also called CRM1), leading to the accumulation of

tumor suppressor proteins in the cell nucleus. This reinitiates and amplifies their tumor suppressor function and is believed to lead to the selective induction of apoptosis in cancer cells, while largely sparing normal cells. To date, over 2,800 patients have been treated with selinexor. In April and September 2018, Karyopharm reported positive data from the Phase 2b STORM study evaluating selinexor in combination with low-dose dexamethasone in patients with penta-refractory multiple myeloma. Selinexor has been granted Orphan Drug Designation in multiple myeloma and Fast Track designation for the patient population evaluated in the STORM study. Karyopharm's New Drug Application (NDA) has been accepted for filing and granted Priority Review by the FDA, and oral selinexor is currently under review by the FDA as a possible new treatment for patients with penta-refractory multiple myeloma. The Company also plans to submit a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) in early 2019 with a request for conditional approval. 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 diffuse large B-cell lymphoma (SADAL), liposarcoma (SEAL), and an investigator-sponsored study 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).

**About Karyopharm Therapeutics**

Karyopharm Therapeutics Inc. (Nasdaq:KPTI) is a clinical-stage pharmaceutical company focused on the discovery and development of novel first-in-class drugs directed against nuclear transport 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). 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, which was founded by Dr. Sharon Shacham, currently 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 our expectations relating to submissions and to the review and potential approval of selinexor by regulatory authorities, including the anticipated timing of such submissions and actions, and the potential availability of accelerated approval pathways, the therapeutic potential of and potential clinical development plans for Karyopharm's drug candidates, especially selinexor, and the plans for commercialization. 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 regulators will agree that selinexor qualifies for accelerated approval in the U.S. or conditional approval in the E.U. as a result of the data from the STORM study in patients with penta-refractory myeloma or the SADAL study in patients with relapsed or refractory DLBCL 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 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: 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; 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, 2018, which was filed with the Securities and Exchange Commission (SEC) on November 8, 2018, 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

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**Karyopharm Reports Updated Selinexor Data from the Phase 2b STORM and Phase 1b/2 STOMP Studies in Relapsed/Refractory Multiple Myeloma at the American Society of Hematology 2018 Annual Meeting**

- *Oral Selinexor Achieves 26.2% Overall Response Rate in STORM Study, 4.4 Month Median Duration of Response, 8.6 Month Median Overall Survival and 15.6 Month Median Survival in Patients with MR or Better –*
- *Once Weekly Oral Selinexor in Combination with Darzalex® and Low Dose Dexamethasone Demonstrates 79% ORR in Patients with Heavily Pretreated, Darzalex®-Naïve, Multiple Myeloma; 73% ORR in the Overall Study Population –*
- *Once Weekly Oral Selinexor in Combination with Oral Pomalyst® and Low Dose Dexamethasone Demonstrates 54% ORR in Pomalyst®-Naïve and Revlimid®-Relapsed or -Refractory Myeloma with 12.2 Month PFS; 50% ORR in the Overall Study Population –*

**NEWTON, Mass.** – December 3, 2018 – Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced presentations highlighting updated data from the Phase 2b STORM study evaluating selinexor, the Company’s first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound, in patients with penta-refractory multiple myeloma, and from two arms of the Phase 1b/2 STOMP study evaluating selinexor and dexamethasone in combination with standard approved therapies, Pomalyst (pomalidomide) or Darzalex (daratumumab), in patients with previously treated multiple myeloma. The data were featured in oral and poster presentations at American Society of Hematology (ASH) 2018 Annual Meeting taking place December 1-4, 2018 in San Diego. A New Drug Application (NDA) seeking accelerated approval for oral selinexor with low dose dexamethasone as a treatment for patients with penta-refractory multiple myeloma is under Priority Review by the U.S. Food and Drug Administration (FDA) with an action date of April 6, 2019, under the Prescription Drug User-Fee Act (PDUFA).

“As an increasing number of myeloma patients experience progressive disease despite treatment with combination regimens, there is a growing need for new therapies, particularly those with novel mechanisms, to help treat patients with relapsed and/or refractory myeloma. The 26.2% ORR determined by the Independent Review Committee (IRC) in the STORM study is highly compelling and reinforces the potential of selinexor in this difficult to treat patient population,” said Sharon Shacham, PhD, MBA, Founder, President and Chief Scientific Officer of Karyopharm. “Additionally, the Phase 1b/2 STOMP study continues to generate encouraging efficacy and safety data from multiple ongoing arms evaluating once weekly oral selinexor and dexamethasone (dex) in combination with the standard approved therapies in patients with newly diagnosed and relapsed/refractory multiple myeloma. The data presented at this year’s ASH annual meeting show impressive response rates across several high unmet need patient subgroups, including Darzalex-naïve or Pomalyst-naïve and Revlimid® (lenalidomide)-relapsed or -refractory myeloma. Given the synergistic activity observed to date with once weekly oral selinexor plus these approved myeloma therapies, we continue to believe that selinexor holds tremendous potential as a future combination backbone therapy in myeloma.”

### Updated Phase 2b STORM Results

These clinical results are from Part 2 of the international, multi-center, single-arm Phase 2b STORM (Selinexor Treatment of Refractory Myeloma) study, which enrolled 122 heavily pretreated patients (median of seven prior treatment regimens) with penta-refractory myeloma. Patients with penta-refractory myeloma have previously received the two proteasome inhibitors (PIs), Velcade® (bortezomib) and Kyprolis® (carfilzomib), the two immunomodulatory drugs (IMiDs), Revlimid® and Pomalyst, and the anti-CD38 monoclonal antibody Darzalex, as well as alkylating agents, and their disease is refractory to glucocorticoids, at least one PI, at least one IMiD, Darzalex and their most recent therapy. Each patient started 80mg oral selinexor twice weekly in combination with low-dose dexamethasone (dex; 20mg twice weekly).

For the STORM study's primary objective, oral selinexor achieved a 26.2% ORR, which included two stringent complete responses (sCRs), six very good partial responses (VGPRs) and 24 partial responses (PRs). The two sCRs were negative for minimal residual disease, one at the level of  $1 \times 10^{-6}$  and one at  $1 \times 10^{-4}$ ; this is particularly significant in this penta-refractory population. Both patients who had relapsed after CAR-T therapy achieved PRs. The ORR in patients who had previously received Darzalex combination therapy (n=86) was 29.1%. The disease control rate for patients who had achieved stable disease or better was 78.7%. All responses were confirmed by an IRC. Median progression-free survival (PFS) was 3.7 months and the median duration of response (DOR) was 4.4 months. Median overall survival (OS) across the study was 8.6 months. Median OS in the approximately 40% of patients with at least a minimum response (MR) on selinexor + dex was 15.6 months compared to a median OS of 1.7 months in patients whose disease progressed or where response was not evaluable ( $p < 0.0001$ ). The short median OS of patients with no response to selinexor is consistent with the lack of available effective therapies for the very heavily pretreated population who entered the study. Real world OS data were also obtained from the Flatiron Health Analytic Database (FHAD). These results further highlight the limited life-expectancy in patients with highly refractory multiple myeloma. OS data from the FHAD indicate that patients with triple-class refractory myeloma (n=69) had a median OS of 3.5 months, also consistent with previously reported data from the literature.

The most common treatment-related adverse events (AEs) were cytopenias, along with gastrointestinal and constitutional symptoms and were consistent with those previously reported from Part 1 of this study (Vogl et al., J Clin Oncol, 2018) and from other selinexor studies. Most were manageable with dose modifications and/or standard supportive care. The most common non-hematologic treatment-related AEs were nausea (69%), fatigue (56%), anorexia (52%), and weight loss (47%) and mostly Grade 1 and 2 events. As expected, the most common Grade 3 and 4 treatment-related AEs were thrombocytopenia (54%), anemia (29%), neutropenia (19%) and fatigue (19%). No significant major organ toxicities were observed, and bleeding and infection rates were low.

Selinexor has been granted Orphan Drug Designation in multiple myeloma and Fast Track designation for the patient population evaluated in the STORM study. A NDA seeking accelerated approval for oral selinexor with low dose dexamethasone as a new treatment for patients with penta-refractory multiple myeloma was accepted and filed with Priority Review by the U.S. FDA. The FDA assigned an action date of April 6, 2019 under the Prescription Drug User-Fee Act (PDUFA). Provided marketing approval is granted by the FDA, Karyopharm plans to commercialize selinexor in the U.S. in the first half of 2019. The Company also plans to submit a Marketing Authorization Application to the European Medicines Agency (EMA) in early 2019 with a request for conditional approval.

**Updated Phase 1b/2 STOMP Study (Selinexor plus Darzalex and Low-dose Dexamethasone (SDd))**

In this arm of the Phase 1b/2 STOMP (Selinexor and Backbone Treatments of Multiple Myeloma Patients) study, oral selinexor (dose escalated using either 100mg once weekly or 60mg twice weekly) is being evaluated in combination with Darzalex (16mg/kg intravenously once weekly) and low dose dexamethasone (dex; 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 PI and an IMiD, or patients with myeloma refractory to both a PI and an IMiD. The following table is a summary of the efficacy results:

Category	Best Responses <sup>1</sup> in Evaluable SDd Patients as of 15-Nov-2018 <sup>2</sup>			
	N <sup>3</sup>	ORR	VGPR	PR <sup>4</sup>
Darzalex naïve	24	19 (79%)	7 (29%)	12 (50%)
All	26	19 (73%)	7 (27%)	12 (46%)

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

- 1 Responses were adjudicated according to the International Myeloma Working Group criteria
- 2 Based on interim unaudited data
- 3 Two patients were not evaluable for response withdrew consent prior to disease follow up
- 4 Two unconfirmed PR

Despite the heavily pretreated nature of the patients in the study, with 100% of the patients having dual- (PI and IMiD) refractory disease, only 19% of patients did not respond (≤stable disease). Median PFS and DOR have not been reached. Based on published data the expected ORR for Darzalex therapy without selinexor in the Darzalex-naïve population is ~30%. Thus, the ORR of 79% provides a basis for further evaluation of the SDd combination.

Among the patients evaluated for safety as of the data cutoff date, the most common treatment-related AEs were cytopenias, along with gastrointestinal and constitutional symptoms; most manageable with dose modifications and/or standard supportive care. The most common non-hematologic treatment-related AEs were nausea (60%), fatigue (48%), diarrhea (32%), vomiting (24%) and anorexia (28%) and mostly Grade 1 and 2 events. As expected, the most common Grade 3 and 4 treatment-related AEs were thrombocytopenia (44%), anemia (28%), leukopenia (28%) and neutropenia (24%). No Grade 5 AEs were reported. The maximum tolerated dose was not reached. Two dose-limiting toxicities (DLTs) (Grade 3 thrombocytopenia and Grade 2 fatigue) were observed in patients receiving selinexor 60mg twice weekly. No DLTs were reported in the 100mg once weekly cohort. The longest duration of therapy is over 60 weeks. Based on these preliminary tolerability and efficacy data, the RP2D of SDd is selinexor (100mg orally, once weekly), Darzalex (16mg/kg, once weekly) and dex (40mg orally, weekly).

**Updated Phase 1b/2 STOMP Study (Selinexor plus 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 dex (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 PI and an IMiD, or patients with myeloma refractory to both a PI and an IMiD. The following table is a summary of the efficacy results:

Prior Therapy Status	Best Responses <sup>1</sup> in Evaluable SPd Patients as of 15-Nov-2018 <sup>2</sup>				
	N <sup>3</sup>	ORR	VGPR	PR <sup>4</sup>	Median PFS
Pomalyst-naïve and Revlimid refractory or relapsed	26	14 (54%)	5 (19%)	9 (35%)	12.2 months
Pomalyst and Revlimid refractory	8	3 (38%)	—	3 (38%)	5.5 months
All	34	17 (50%)	5 (15%)	12 (35%)	12.2 months

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

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

Responses tended to occur rapidly with a median of one month to onset. Median PFS among all evaluable patients was 12.2 months, with a follow up of 9.4 months. Median PFS in Pomalyst and Revlimid-refractory myeloma was 5.5 months. Among patients with a PR or better (n=17), the median time on treatment was 9.4 months.

Among the patients evaluated for safety as of the data cutoff date, the most common treatment-related AEs were cytopenias, along with gastrointestinal and constitutional symptoms; most manageable with dose modifications and/or standard supportive care. The most common non-hematologic treatment-related AEs were nausea (53%), fatigue (50%) and weight decreased (34%). As expected, the most common treatment-related Grade 3 and 4 AEs were neutropenia (55%), thrombocytopenia (34%), anemia (29%) and leukopenia (18%). There were three Grade 5 treatment-related events (febrile neutropenia, intracranial hemorrhage and pneumonia). Based on these tolerability and efficacy data, doses of oral selinexor 60-80mg once weekly are being evaluated in combination with Pomalyst (3mg orally, once daily) and low dose dex to determine the RP2D for this combination regimen.

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 proteasome inhibitor Velcade and dex (SVd) for the treatment of patients with multiple myeloma who have had one to three prior lines of therapy. The Company expects to complete enrollment in the BOSTON study by the end of 2018, with top-line data anticipated at the end of 2019. Assuming a positive outcome, Karyopharm plans to use the results from the BOSTON study to support an application for full approval of selinexor in relapsed/refractory multiple myeloma.

**Details for the ASH 2018 presentations highlighting the STORM and STOMP studies are as follows:**

**Title:** Results of the Pivotal STORM Study (Part 2) in Penta-Refractory Multiple Myeloma (MM): Deep and Durable Responses with Oral Selinexor Plus Low Dose Dexamethasone in Patients with Penta-Refractory MM

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

**Abstract Number/Publication ID:** 598

**Session:** 653. **Myeloma:** Therapy, excluding Transplantation: Antibodies and Targeted Therapies

**Date and Time:** Monday, December 3, 2018; 7:45 AM PT

**Location:** San Diego Convention Center, Room 6F

**Title:** Deep and Durable Responses with Selinexor, Daratumumab, and Dexamethasone (SDd) in Patients with Multiple Myeloma (MM) Previously Exposed to Proteasome Inhibitors and Immunomodulatory Drugs: Results of Phase 1b Study of SDd

**Presenter:** Cristina Gasparetto, Duke University Cancer Center, Durham, North Carolina

**Abstract Number/Publication ID:** 599**Session:** 653. Myeloma: Therapy, excluding Transplantation: Antibodies and Targeted Therapies**Date and Time:** Monday, December 3, 2018; 8:00 AM PT**Location:** San Diego Convention Center, Room 6F**Title:** Selinexor Plus Pomalidomide and Low Dose Dexamethasone (SPd) in Patients with Relapsed or Refractory Multiple Myeloma**Presenter:** Christine Chen, Princess Margaret Cancer Center, Toronto, Ontario**Abstract Number/Publication ID:** 1993**Session:** 653. Myeloma: Therapy, excluding Transplantation: Poster I**Date and Time:** Saturday, December 1, 2018; 6:15-8:15 PM PT**Location:** San Diego Convention Center, Hall GH**About Selinexor**

Selinexor is a first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound. Selinexor functions by binding with and inhibiting the nuclear export protein XPO1 (also called CRM1), leading to the accumulation of tumor suppressor proteins in the cell nucleus. This reinitiates and amplifies their tumor suppressor function and is believed to lead to the selective induction of apoptosis in cancer cells, while largely sparing normal cells. To date, over 2,800 patients have been treated with selinexor. In April and September 2018, Karyopharm reported positive data from the Phase 2b STORM study evaluating selinexor in combination with low-dose dexamethasone in patients with penta-refractory multiple myeloma. Selinexor has been granted Orphan Drug Designation in multiple myeloma and Fast Track designation for the patient population evaluated in the STORM study. Karyopharm's New Drug Application (NDA) has been accepted for filing and granted Priority Review by the FDA, and oral selinexor is currently under review by the FDA as a possible new treatment for patients with penta-refractory multiple myeloma. The Company also plans to submit a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) in early 2019 with a request for conditional approval. 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 diffuse large B-cell lymphoma (SADAL), liposarcoma (SEAL), and an investigator-sponsored study 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).

**About Karyopharm Therapeutics**

Karyopharm Therapeutics Inc. (Nasdaq:KPTI) is a clinical-stage pharmaceutical company focused on the discovery and development of novel first-in-class drugs directed against nuclear transport 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). 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, which was founded by Dr. Sharon Shacham, currently 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 our expectations relating to submissions and to the review and potential approval of selinexor by regulatory authorities, including the anticipated timing of such submissions and actions, and the potential availability of accelerated approval pathways, the therapeutic potential of and potential clinical development plans for Karyopharm's drug candidates, especially selinexor, and the plans for commercialization. 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 regulators will agree that selinexor qualifies for accelerated approval in the U.S. or conditional approval in the E.U. as a result of the data from the STORM study in patients with penta-refractory myeloma or the SADAL study in patients with relapsed or refractory DLBCL 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 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: 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; 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, 2018, which was filed with the Securities and Exchange Commission (SEC) on November 8, 2018, 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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