UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 8-K

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

Date of report (Date of earliest event reported): June 14, 2019

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

Delaware	001-36167	26-3931704
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

85 Wells Avenue, 2nd Floor Newton, Massachusetts	02459
(Address of Principal Executive Offices)	(Zip Code)

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

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

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. ☐

Item 8.01. Other Events.

On June 14, 2019, Karyopharm Therapeutics Inc. issued a press release announcing the presentation of new clinical data from one treatment arm and updated clinical data from two treatment arms of the Phase 1b/2 STOMP study at the European Hematology Association Annual Congress.

A copy of the press release is filed as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

99.1 Press release issued by Karyopharm Therapeutics Inc. on June 14, 2019

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: June 14, 2019

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

Karyopharm Reports New and Updated Selinexor Combination Data from the Phase 1b/2 STOMP Study at the European Hematology Association 2019 Annual Meeting

– Once Weekly Oral Selinexor in Combination with Kyprolis® and Low Dose Dexamethasone Demonstrates 78% ORR in Patients with Heavily Pretreated, Kyprolis-Naïve Multiple Myeloma –

– Once Weekly Oral Selinexor in Combination with Darzalex® and Low Dose Dexamethasone Demonstrates 73% ORR in Patients with Heavily Pretreated, Darzalex-Naïve Multiple Myeloma –

– Once Weekly Oral Selinexor in Combination with Oral Pomalyst® and Low Dose Dexamethasone Demonstrates 57% ORR in Pomalyst-Naïve and Revlimid®-Relapsed or -Refractory Multiple Myeloma with 12.2 Month PFS –

NEWTON, Mass. – June 14, 2019 – Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced three presentations highlighting new and updated data from the Phase 1b/2 STOMP (**S**elinexor and Backbone **T**reatments **o**f Multiple **M**yeloma **P**atients) study evaluating selinexor, the Company's first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound, and dexamethasone in combination with standard approved multiple myeloma (MM) therapies, Kyprolis® (carfilzomib), Darzalex® (daratumumab), or Pomalyst® (pomalidomide), in patients with previously treated multiple myeloma. The data will be featured in oral and poster presentations at the European Hematology Association (EHA) 2019 Annual Meeting taking place June 13-16, 2019 in Amsterdam.

"Preliminary data from the Kyprolis arm of the Phase 1b/2 STOMP study show early but encouraging clinical activity, including two patients who achieved a complete response, along with an expected and manageable tolerability profile, in patients with heavily pretreated, double-refractory Kyprolis-naïve multiple myeloma," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "Additionally, the Darzalex and Pomalyst arms of the STOMP study continue to demonstrate impressive response rates, including encouraging rates of very good partial responses (VGPR), which indicate a 90% or greater reduction in a patient's disease burden."

New Phase 1b/2 STOMP Study Data: Selinexor plus Kyprolis and Low-dose Dexamethasone (SKd)

In this arm of the Phase 1b/2 STOMP study, oral selinexor (dosed once weekly) is being evaluated in combination with Kyprolis (56mg/m^2 or 70mg/m^2 once weekly) and low dose dex (orally, 40mg once weekly or 20mg twice weekly) in patients with relapsed refractory MM who have received at least two prior therapies, which can include previous treatment with a proteasome inhibitor (PI), one or more immunomodulatory drugs (IMiDs: Revlimid, Pomalyst) or Darzalex. All patients on the study had previously received both PIs and IMiDs. The following table is a summary of the efficacy results:

Best Responses[1] in Evaluable SKd Patients as of 1-May-2019[2]

Category	N	ORR	CR	VGPR	SD
All (Kyprolis-naïve)	9	7 (78%)	2 (22%)	5 (56%)	2 (22%)

Key: ORR=Overall Response Rate (CR+VGPR+PR); SD= Stable Disease

1 Responses were adjudicated according to the International Myeloma Working Group criteria
2 Based on interim unaudited data

Among the 9 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 were manageable with dose modifications and/or standard supportive care. The most common non-hematologic treatment-related AEs were nausea (67%), fatigue (44%), hyperglycemia (44%), anorexia (33%) and vomiting (33%), and were mostly Grade 1 and 2 events. As expected, the most common treatment-related Grade 3 and 4 AEs were hematologic AEs and included thrombocytopenia (78%), leukopenia (33%), anemia (22%) and neutropenia (22%). Dose limiting toxicities, including Grades 3 and 4 thrombocytopenia, Grade 3 pneumonia and Grade 3 vomiting, were observed in patients receiving selinexor 80mg and Kyprolis 70mg/m^2 and selinexor 100mg and Kyprolis 56mg/m^2. No DLTs were reported in the selinexor 80mg and Kyprolis 56mg/m^2 cohort, and therefore, confirmation of the recommended Phase 2 dose (RP2D) is ongoing with this dosing regimen.

Updates on Phase 1b/2 STOMP Study: SDd and SPd

Selinexor plus Darzalex and Low-dose Dexamethasone (SDd)

In this arm of the Phase 1b/2 STOMP 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 MM who received at least three prior lines of therapy, including a PI and an IMiD, or patients with MM refractory to both a PI and an IMiD. The following table is a summary of the updated efficacy results:

Best Responses[1] in Evaluable SDd Patients as of 1-May-2019[2]

Category	N[3]	ORR	VGPR	PR[4]
Darzalex naïve	30	22 (73%)	11 (37%)	11 (37%)
All	32	22 (69%)	11 (34%)	11 (34%)

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

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 as they withdrew consent prior to disease follow up
4 Two unconfirmed PRs

Despite the heavily pretreated nature of the patients in the study, with 100% of the patients having dual- (PI and IMID)-refractory disease, only one patient (3%) did not have at least a minimal response. Median progression-free survival (PFS) has not been reached. Among patients with at least a PR, the median time on treatment was 7.7 months, while the median time on study for all evaluable patients was 4.8 months. Median time to response was 1.0 month. Based on published data, the expected ORR for Darzalex therapy without selinexor in the Darzalex-naïve population is ~29%. Thus, the ORR of 73% continues to provide a basis for further evaluation of the SDd combination.

Among the 31 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 (68%), fatigue (58%), anorexia (32%), insomnia (32%), diarrhea (32%), hyponatremia (32%), and vomiting (26%), and were mostly Grade 1 and 2 events. As expected, the most common Grade 3 and 4 treatment-related AEs were hematologic AEs and included thrombocytopenia (42%), anemia (29%), leukopenia (26%) and neutropenia (23%). No Grade 5 AEs were reported. Based on these tolerability and efficacy data, the recommended RP2D of SDd is selinexor (100mg orally, once weekly), Darzalex (16mg/kg, once weekly) and dex (40mg orally, once weekly).

Selinexor plus Pomalyst and Low-dose Dexamethasone (SPd)

In this arm of the Phase 1b/2 STOMP study, oral selinexor (60mg or 80mg once weekly or 60mg or 80mg twice weekly) is being evaluated in combination with Pomalyst (2mg, 3mg or 4mg orally, once daily) and low dose dex (orally, 40mg once weekly or 20mg twice weekly) in patients with relapsed or refractory MM who received at least two prior lines of therapy, including a PI and an IMiD, or patients with MM refractory to both a PI and an IMiD. The following table is a summary of the efficacy results:

Best Responses[1] in Evaluable SPd Patients as of 1-May-2019[2]

Prior Therapy Status	N[3]	ORR	VGPR	PR[4]	Median PFS
Pomalyst-*naïve* and Revlimid refractory or relapsed	30	17 (57%)	7 (23%)	10 (33%)	12.2 months
Pomalyst *and* Revlimid refractory	10	3 (30%)	—	3 (30%)	4.2 months
All	40	20 (50%)	7 (18%)	13 (33%)	10.4 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 Five patients not evaluable for response: one death unrelated to myeloma, one non-compliance with study procedures, two withdrawal of consent before disease follow up, one patient on treatment pending response evaluation
4 One unconfirmed PR

Among the 45 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 (56%), fatigue (53%) and anorexia (49%) and mostly Grade 1 and 2 events. As expected, the most common treatment-related Grade 3 and 4 AEs were hematologic AEs and included neutropenia (56%), thrombocytopenia (31%), anemia (31%) and leukopenia (16%). There were three Grade 5 treatment-related events (febrile neutropenia, intracranial hemorrhage and pneumonia). Determination of the RP2D is still ongoing.

Details for the EHA 2019 STOMP presentations are as follows:

Oral Presentation

Title: Safety and Efficacy of combination of Selinexor, Daratumumab, and Dexamethasone (SDd) in Patients with Multiple Myeloma (MM) Previously Exposed to Proteasome Inhibitors and Immunomodulatory Drugs
Lead author: Cristina Gasparetto, Duke University Cancer Center
Abstract #: S1606
Session: Myeloma and other monoclonal gammopathies – Clinical
Date and Time: Sunday, June 16, 2019; 09:00 – 09:15 CEST
Location: Auditorium

Poster Presentations

Title: Selinexor, Pomalidomide, and Dexamethasone (SPd) in Patients with Relapsed or Refractory Multiple Myeloma (RRMM)
Lead author: Christina Chen, Princess Margaret Cancer Center
Abstract #: PF587
Session: Myeloma and other monoclonal gammopathies – Clinical
Date and Time: Friday, June 14, 2019; 17:30 – 19:00 CEST

Location: Poster Area

Title: A Phase 1b/2 Study of Selinexor, Carfilzomib, and Dexamethasone (SKd) in Relapsed/ Refractory Multiple Myeloma (RRMM)
Lead author: Cristina Gasparetto, Duke University Cancer Center
Abstract #: PS1414
Session: Myeloma and other monoclonal gammopathies – Clinical
Date and Time: Saturday, June 15, 2019; 17:30 – 19:00 CEST
Location: Poster Area

Additional selinexor presentations at EHA 2019 are as follows:

Title: A Phase 2 Study of Selinexor Plus Cytarabine and Idarubicin in Patients with Relapsed/Refractory Acute Myeloid Leukemia (AML)
Lead author: Walter Fiedler, Hubertus Wald University Cancer Center Hamburg
Abstract #: S880
Session: Acute myeloid leukemia – Clinical
Date and Time: Saturday, June 15, 2019; 17:00 – 17:15 CEST
Location: Elicium 2

Title: A Randomized, Open-Label, Phase II Study of Selinexor Versus Physician's Choice (PC) In Older Patients with Relapsed or Refractory Acute Myeloid Leukemia (AML)
Lead author: Kendra Sweet, Moffitt Cancer Center
Abstract #: PF261
Session: Acute myeloid leukemia – Clinical
Date and Time: Friday, June 14, 2019; 17:30 – 19:00 CEST
Location: Poster Area

Note: As reported previously by Karyopharm in 2017, this study did not meet its pre-specified primary endpoint.

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. In 2018, Karyopharm reported positive data from the Phase 2b STORM study evaluating selinexor in combination with low-dose dexamethasone in patients with triple class refractory multiple myeloma who have been previously exposed to all five of the most commonly prescribed anti-myeloma therapies currently available. 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) seeking accelerated approval 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 based on data from the STORM study. The Company has also submitted a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) with a request for conditional approval. 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), 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.

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.

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 to, and 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 our clinical data, including the data from the STORM study 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 March 31, 2019, which was filed

with the Securities and Exchange Commission (SEC) on May 9, 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.
Darzalex® is a registered trademark of Janssen Biotech, Inc.

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