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):
December 10, 2017

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))

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 December 10, 2017, Karyopharm Therapeutics Inc. issued a press release announcing the presentation of clinical data from four arms of the ongoing Phase 1b/2 STOMP study at the American Society of Hematology 2017 annual meeting.

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 December 10, 2017

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 11, 2017

By: /s/ Christopher B. Primiano
Christopher B. Primiano
Senior Vice President, Operations, Business Development, General Counsel and Secretary

Karyopharm Presents Positive Selinexor Data from the Phase 1b/2 STOMP Study at the American Society of Hematology 2017 Annual Meeting

– Data Provide Further Evidence of Tolerability with Robust Anti-Myeloma Activity When Selinexor is Combined with Velcade, Pomalyst, Revlimid or Darzalex –

– SVd Arm Continues to Show High Response Rates, Including 83% ORR and >13-month PFS in BOSTON Patient Population; 63% ORR in the Overall Study Population –

– SPd Arm Also Demonstrating Strong Response Rates, Including 63% ORR in Pomalyst-Naïve and Revlimid-Relapsed or -Refractory Patients and 56% ORR in the Overall Study Population –

NEWTON, Mass. – December 10, 2017 – Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced the presentation of four posters highlighting clinical data from the ongoing Phase 1b/2 STOMP study at the American Society of Hematology (ASH) 2017 annual meeting held December 9-12, 2017 in Atlanta. The STOMP study is evaluating selinexor, the Company's lead, novel, oral SINE compound, in combination with backbone therapies for the treatment of patients with heavily pretreated multiple myeloma (MM). Two of the presentations feature updated data from the STOMP arms evaluating selinexor plus low dose dexamethasone (Sd) in combination with either Velcade® (bortezomib) (SVd), or Pomalyst® (pomalidomide) (SPd). The other two presentations feature new data from the STOMP arms evaluating Sd with Revlimid® (lenalidomide) (SRd) and with Darzalex® (daratumumab) (SDd).

"The results from the SVd arm of the Phase 1b/2 STOMP study, particularly the high response rates of 83% in the same patient population eligible for the BOSTON study and 84% in proteasome inhibitor (PI)-naïve or PI-relapsed patients, together with prolonged progression-free survival (PFS), strongly support our ongoing, pivotal Phase 3 BOSTON study," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "Overall, the four presentations continue to highlight evidence of strong activity when oral selinexor is combined with the currently available "backbone" myeloma therapies, including PIs, immunomodulatory drugs (IMiDs) and anti-CD38 monoclonal antibodies. Oral selinexor continues to demonstrate an expected and manageable tolerability profile, particularly in the SVd regimen where the combination produced higher response rates, paired with lower rates of peripheral neuropathy (PN), compared to the commonly used regimen of Velcade plus dexamethasone. We are delighted to share the results of this research with the medical community at ASH this year."

Selinexor in Combination with Velcade and Low-dose Dexamethasone (SVd)

In the poster presentation titled, "Selinexor in combination with weekly low dose bortezomib and dexamethasone (SVd) induces a high response rate with durable responses in patients with refractory multiple myeloma," (Abstract #3135) Nizar Bahlis, MD, Southern Alberta Cancer Research Institute, presented updated clinical data from the SVd arm of the STOMP study. The study included patients whose disease was PI naïve, exposed or refractory, provided their disease was not refractory to Velcade as a last

therapy. In this study arm, oral selinexor was dose-escalated in once-weekly (80 or 100mg) or twice-weekly (60 or 80mg) regimens. Velcade (1.3mg/m2 subcutaneously) was administered once-weekly or twice-weekly. Dexamethasone (dex) was administered orally either 40mg once-weekly or 20mg twice-weekly. The following table is a summary of the efficacy results:

Best Responses[1] in Evaluable SVd Patients as of 15-Nov-2017[2]

Category	N[3]	ORR (%)	CR	VGPR	PR[4]	Median PFS
PI Relapsed/Naïve	19	**16 (84%)**	2 (11%)	5 (26%)	9 (47%)	>13 months
PI Relapse/Naïve, ≤3 Prior Treatments (BOSTON[5])	18	**15 (83%)**	2 (11%)	6 (33%)	7 (39%)	
PI Refractory (Velcade, Kyprolis, Ninlaro)	21	**9 (43%)**	1 (5%)	4 (19%)	4 (19%)	6.4 months
All	40	**25 (63%)**	3 (8%)	9 (23%)	13 (33%)	9.0 months

Key: ORR=Overall Response Rate (CR+VGPR+PR), CR=Complete Response, 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 Two patients not evaluable for response: one death unrelated to myeloma and one withdrawal of consent before disease follow up
4 One unconfirmed PR
5 Patient population eligible for the ongoing Phase 3, randomized BOSTON study evaluating SVd versus Vd

The majority of patients had reductions in M-protein, including 33% with a ≥90% reduction. In the PI Relapsed/Naïve population (N=19), the ORR was 84% and the median PFS was >13 months with similar results in the "BOSTON" population (N=18). This compares favorably to standard Vd regimens (the control arm of the BOSTON study) with ORR 60-65% and PFS 7-9 months across many previous studies.

Adverse events were consistent with those reported previously from the SVd arm of the STOMP study with nausea, anorexia, fatigue, diarrhea and vomiting the most commonly reported for Grade 1/2. Importantly, the reported PN across all patients was Grade 1/2 and limited to six patients (14%), of which five had prior Velcade exposure. Grade ≥3 adverse events were also consistent with those reported previously with thrombocytopenia, neutropenia, fatigue and anemia being the most common. The recommended Phase 2 dose (RP2D) regimen for SVd is oral selinexor (100mg once weekly), Velcade (1.3mg/m2 once-weekly subcutaneously) and oral dex (40mg once weekly), which represents 40% less Velcade and 25% less dex compared to the approved standard Velcade + dex (Vd) regimen.

Dr. Bahlis commented, "These updated data continue to support the thesis that selinexor combined with once-weekly Velcade and low-dose dex is well tolerated and highly active in relapsed or refractory myeloma. The high response rates and durability observed with SVd are achieved with 40% less Velcade and 25% less dex, with no overt major organ toxicities. The SVd response rates in patients with PI non-refractory myeloma, together with the low rate of PN, compares favorably to the response rates and much higher PN reported from other late-stage Vd trials. In patients with PI refractory myeloma, the response rates reported here support prior preclinical findings suggesting selinexor's potential to re-sensitize myeloma to PIs."

Selinexor in Combination with Pomalyst and Low-dose Dexamethasone (SPd)

In the poster presentation titled, "Selinexor in Combination with Pomalidomide and Low Dose Dexamethasone in a Relapsed / Refractory Multiple Myeloma Patient Population with Prior Proteasome Inhibitor and Lenalidomide Exposure," (Abstract #3136) Christine Chen, MD, FRCP, University of Toronto, Princess Margaret Cancer Center, presented updated clinical data from the SPd arm of the STOMP study which includes MM patients who previously received Revlimid and a PI. In this study arm, selinexor was dosed orally either once weekly (60 or 80mg) or twice weekly (60 or 80mg) with Pomalyst (4mg orally, once daily) and dex (orally, 40mg once weekly or 20mg twice weekly). The following table is a summary of the efficacy results:

Best Responses[1] in Evaluable SPd Patients as of 15-Nov-2017[2]

Category	N[3]	ORR (%)	VGPR	PR[4]	Median PFS
Pomalyst Naïve and Revlimid Refractory or Relapsed	19	**12 (63%)**	2 (11%)	10 (53%)	11.6 months
Pomalyst and Revlimid Refractory	8	**3 (38%)**	—	3 (38%)	4.8 months
All	27	**15 (56%)**	2 (7%)	13 (48%)	11.6 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 withdrawals 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 of 11.6 for SPd compares favorably with the PFS of ~4 months reported for Pomalyst-dex in the Revlimid refractory or relapsed population.

Among the 31 patients evaluable for safety, the most common Grade 1/2 adverse events were nausea (52%), anorexia (45%), fatigue (45%) and diarrhea (32%). The most common Grade ≥3 adverse events were neutropenia (55%), thrombocytopenia (32%) and anemia (29%). Gastrointestinal adverse events were generally manageable with antiemetics. There were two Grade 5 treatment-related events (febrile neutropenia and intracranial hemorrhage). Five DLTs (Grade 3 fatigue, neutropenia and febrile neutropenia) were observed in patients receiving selinexor 60mg twice weekly and 80mg once weekly. Based on the activity and tolerability observed in this study arm, 60-80mg of oral selinexor 60mg 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.

Dr. Chen commented, "Myeloma patients whose disease is refractory to a PI and an IMiD would typically move to the currently approved regimen of Pomalyst and dex, which carries an expected ORR of up to 30% and PFS of approximately four months in this patient population. The 56% ORR reported here shows the significant clinical activity of this novel, all oral, SPd regimen in patients with heavily pretreated myeloma. These data continue to build upon the body of clinical data suggesting that once-weekly selinexor is generally well tolerated and can rapidly induce durable responses when combined with Pomalyst and dex in patients with PI- and Revlimid-exposed myeloma, including patients whose disease was refractory to prior therapy with Pomalyst. This SPd regimen has the potential to provide a new therapeutic option for myeloma patients where a significant unmet need remains."

Selinexor in Combination with Revlimid and Low-dose Dexamethasone (SRd)

In the poster presentation titled, "A Phase Ib/II Trial of Selinexor Combined with Lenalidomide and Low Dose Dexamethasone in Patients with Relapsed / Refractory Multiple Myeloma," (Abstract #1861) Darrell White, MD, Dalhousie University and QEII Health Sciences Center, presented new clinical data from the SRd arm of the STOMP study evaluating patients who received at least one prior therapy, which may include prior Revlimid, as long as the patient's MM was not refractory to prior Revlimid. Patients whose MM was refractory to Revlimid maintenance regimens were also allowed in this cohort. In this study arm, oral selinexor was dose-escalated starting at either 60mg once weekly or 60mg twice weekly, with Revlimid (25mg orally, once daily), and dex (orally, 40mg once weekly or 20mg twice weekly). The following table is a summary of the efficacy results:

Best Responses[1] in Evaluable SRd Patients as of 15-Nov-2017[2]

Category	N[3]	ORR	VGPR	PR[4]
Revlimid Naïve (All)	12	11 (92%)	3 (25%)	8 (67%)
Revlimid Naïve, ≤2 Prior Treatments	10	10 (100%)	3 (30%)	7 (70%)
Revlimid Relapsed or Refractory	4	2 (50%)	—	2 (50%)
All	16	13 (81%)	3 (19%)	10 (63%)

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 Three patients not evaluable for response: two deaths unrelated to myeloma, one withdrawal of consent before disease follow up
4 Three unconfirmed PRs

Median PFS for the overall study population and for patients with Revlimid-naïve disease was not reached. The median time on treatment for the overall study population was not reached.

Among the 19 patients evaluable for safety, the most common Grade 1/2 adverse events were nausea (68%), anorexia (42%), fatigue (42%), weight loss (42%), constipation (32%) and vomiting (32%). The most common Grade □3 adverse events were thrombocytopenia (68%) and neutropenia (58%). Gastrointestinal adverse events were generally manageable with antiemetics. Five DLTs (thrombocytopenia (n=4) and anorexia (n=1)) were observed in patients receiving selinexor 60mg twice weekly and 80mg once weekly. Thrombocytopenia and anorexia were reduced in the selinexor 60mg once weekly cohort versus the twice weekly groups. Based on the activity and tolerability observed in this study arm, the RP2D of the all-oral SRd is selinexor (60mg orally, once weekly), Revlimid (25mg orally, once daily) and dex (40mg orally, once weekly).

Dr. White commented, "These Phase 1 results suggest that selinexor can be safely combined with Revlimid and dex in an all oral regimen in patients with relapsed or refractory myeloma who have received at least one prior therapy. We were especially pleased to see an encouraging 81% response rate across all patients and a 92% response rate in patients with Revlimid-naïve disease, clear signals of clinical activity, with no new or unexpected toxicities observed. Importantly, this combination shows no evidence of cardiac, pulmonary, liver or renal toxicity. We look forward to continuing our evaluation of selinexor in this SRd regimen in patients with relapsed or refractory myeloma."

Selinexor in Combination with Darzalex and Low-dose Dexamethasone (SDd)

In the poster presentation titled, "A Phase 1b Study to Assess the Combination of Selinexor and Daratumumab in Patients with Relapsed/Refractory Multiple Myeloma Previously Exposed to Proteasome Inhibitors (PI) and Immunomodulatory Drugs," (Abstract #3100) Cristina Gasparetto, MD, Duke University Cancer Center, presented new clinical data from the SDd arm of the STOMP study evaluating MM patients 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. In this study arm, oral selinexor was dose escalated using either 100mg once weekly or 60mg twice weekly, with Darzalex (16mg/kg intravenously once weekly) and dex (orally, 40mg once weekly or 20mg twice weekly). The following table is a summary of the efficacy results:

Best Responses[1] in Evaluable SDd Patients as of 15-Nov-2017[2]

Category	N[3]	ORR	VGPR	PR[4]
Darzalex Naïve	6	5 (83%)	3 (50%)	2 (33%)
All	8	5 (63%)	3 (38%)	2 (25%)

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 One patient not evaluable for response withdrew consent prior to disease follow up due to severe infusion reaction associated with Darzalex
4 One unconfirmed PR

Four of nine patients remain on treatment. Responses tended to occur rapidly with a median of one month to onset. Among the nine patients evaluable for safety, the most common Grade 1/2 adverse events were fatigue (44%), nausea (33%) and neutropenia (33%). The most common Grade 3/4 adverse events were thrombocytopenia (56%), leukopenia (44%), anemia (44%) and neutropenia (33%). Gastrointestinal adverse events were generally manageable with antiemetics. The maximum tolerated dose was not reached. Two DLTs (Grade 3 thrombocytopenia and Grade 2 fatigue) were observed in patients receiving selinexor 60mg twice weekly; both patients showed responses. Based on the preliminary tolerability and efficacy data, the RP2D of SDd is selinexor (100mg orally, once weekly), Darzalex (16mg/kg, once weekly) and dex (40mg orally, once weekly).

"Preclinical results have shown that oral selinexor sensitizes patients' myeloma cells to the anti-CD38 monoclonal antibody, Darzalex," stated Dr. Gasparetto. "These Phase 1b data are early but encouraging, and suggest that selinexor can be safely combined with Darzalex and low-dose dexamethasone in patients with heavily pretreated myeloma. The responses observed occur rapidly within a median one cycle of treatment. We look forward to further evaluating the SDd combination."

About Selinexor

Selinexor (KPT-330) 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 2,200 patients have been treated with selinexor, and it is currently being evaluated in several 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), in combination with low-dose dexamethasone (STORM) and backbone therapies (STOMP), and in diffuse large B-cell lymphoma (SADAL), and liposarcoma (SEAL), among others. Additional Phase 1, Phase 2 and Phase 3 studies are ongoing or currently planned, including multiple studies in combination with one or more 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 the therapeutic potential of and potential clinical development plans for Karyopharm's drug candidates. Such statements are subject to

numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from Karyopharm's current expectations. For example, there can be no guarantee that any of Karyopharm's SINE compounds, including selinexor or eltanexor (KPT-8602), will successfully complete necessary preclinical and 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, 2017, which was filed with the Securities and Exchange Commission (SEC) on November 2, 2017, 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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Revlimid® and Pomalyst® are registered trademarks of Celgene Corporation.
Darzalex® is a registered trademark of Janssen Biotech, Inc.

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