August 10, 2015

Karyopharm Reports Second Quarter 2015 Financial Results and Highlights Recent Progress

- Positive Selinexor Clinical Data Presented across Several Difficult to Treat Cancers -

- Provides Update to Certain Trials based on Expanding Clinical Experience -

Conference Call Scheduled for today at 8:30 a.m. ET

NEWTON, Mass., Aug. 10, 2015 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today reported financial results for the second quarter 2015 and commented on recent accomplishments and clinical development plans for selinexor, its lead product candidate.

"Important data describing the clinical benefit of selinexor across multiple solid and hematologic malignancies was presented during the quarter, including single agent anti-tumor activity and durable disease control in patients with recurrent glioblastoma, advanced sarcomas, ovarian and endometrial cancers. We also presented survival data in patients with relapsed/refractory diffuse large B-cell lymphoma treated with selinexor, along with combination data of selinexor with chemotherapy in patients with heavily pretreated acute myeloid leukemia," said Michael G. Kauffman, MD, PhD, Chief Executive Officer of Karyopharm. "In addition, we continue to execute against the selinexor clinical development plan with the initiation of a Phase 2 study in patients with quad-refractory multiple myeloma and make steady progress enrolling patients in our other on-going later phase clinical trials in acute myeloid leukemia, diffuse large B cell lymphoma and Richter's transformation. Furthermore, we made some important changes to certain trials based on our growing experience with selinexor. Finally, we recently met with FDA and now have a path forward for a phase 2/3 study in liposarcoma. In the second half of 2016, we look forward to reporting preliminary top-line data from our later phase clinical trials in AML, DLBCL and Richter's transformation, as well as data from the first 80 patients in our later phase clinical trial in multiple myeloma in the middle of 2016."

Conference Call Information:

To access the conference call, please dial (855) 437-4406 (US) or (484) 756-4292 (international) at least five minutes prior to the start time and refer to conference ID 98056569. A live audio webcast of the call will be available under "Events & Presentations" in the Investor section of Karyopharm's website, http://www.karyopharm.com, approximately two hours after the event.

Scientific Presentations and Publications:

- Presented positive clinical data with single-agent, oral selinexor in on-going Phase 2 and Phase 1b clinical studies across multiple solid tumors at the 2015 American Society of Clinical Oncology (ASCO) Annual Meeting including anti-tumor activity and disease control in patients with recurrent glioblastoma, advanced sarcomas, heavily pre-treated gynecological cancers and across multiple malignancies in Asian patients, including:
  - anti-tumor activity, including brain penetration at clinically relevant drug levels, with a 13% overall response rate (ORR) and a 38% disease control rate (DCR) in patients with recurrent glioblastoma in an ongoing Phase 2 clinical trial;
  - durable activity, including longer progression free survival (PFS) than last prior regimen, in an ongoing Phase 1b clinical study in patients with advanced sarcomas, including liposarcoma;
  - promising anti-tumor activity or disease control across ovarian, endometrial and cervical cancers with disease control rates (DCR) of up to 62% and several patients remaining on study for up to 12 months in an ongoing Phase 2 clinical trial in patients with heavily pre-treated, progressive gynecological cancers;
  - anti-tumor activity across a variety of malignancies in a Phase 1 clinical trial evaluating the activity of selinexor in Asian patients with advanced malignancies.
- Presented clinical data with oral selinexor, both as single agent and in combination with chemotherapy, in a number of hematologic malignancies including diffuse large B-cell lymphoma (DLBCL) and acute myeloid leukemia (AML) at the 20th Congress of the European Hematology Association (EHA) 2015 Annual Meeting, including:
  - updated survival data from an ongoing Phase 1b clinical trial of single-agent selinexor in heavily pre-treated patients with DLBCL in which patients with a response to selinexor (N=12) demonstrated a median overall survival (OS) of greater than 10 months (median not reached) and PFS was 24 months, significantly longer than those without a response (N=27; OS 3.5 months, PFS 1.2 months);

- preliminary Phase 2 results from an ongoing clinical trial of selinexor in combination with chemotherapy (idarubicin/Ara-C) in 18 evaluable patients with relapsed or refractory AML demonstrated a 56% ORR, including nine patients with complete remission (CR/CRi) and one patient with a partial remission (PR).

- Presented clinical and preclinical data with single agent, oral selinexor at the 13th International Conference on Malignant Lymphoma (ICML) in DLBCL patients with MYC, BCL2 and/or BCL6 translocations, so called "Double Hit and Triple Hit" Lymphomas -- areas of significant unmet medical need associated with poor prognosis and limited standard-of-care treatment options:
  - In an ongoing Phase 1 clinical trial in 14 relapsed, refractory DLBCL patients with triple, double or single hit MYC, BCL2 and/or BCL6 translocations, selinexor demonstrated clinically meaningful activity with a 43% ORR (PR or better) including two CRs, four PRs and two additional patients achieving stable disease (SD).
  - In preclinical models, selinexor demonstrated potency in double hit DLBCL cell lines in vitro and in an aggressive derived xenograft (PDX) model of triple hit DLBCL, with 84% tumor growth inhibition.

Regulatory and Intellectual Property Updates:

- Karyopharm met with the FDA in July and plans to initiate a Phase 2/3 clinical trial of selinexor versus placebo to treat liposarcoma in the second half of 2015. Accrual to Karyopharm's Phase 1b clinical trial in sarcomas, including liposarcoma, is nearly complete.
- Granted U.S. patent for KPT-350, an oral SINE™ compound being developed for the treatment of inflammatory and autoimmune diseases. This patent, which will expire in 2033 absent any patent term extensions, covers the composition of matter for KPT-350, as well as certain other compositions and related methods.
- Granted U.S. patent covering method of treatment using certain SINE™ compounds, including selinexor and verdinexor. This patent will expire in 2032 absent any patent term extensions, and the covered methods of treatment include methods for treating viral infections, inflammatory disorders and cancer.

Clinical Development Plans:

- Karyopharm initiated a single-arm trial in multiple myeloma called STORM, for **S**elinexor **T**reatment **o**f **R**efractory **M**yeloma, which will initially include 80 patients. If the data from the initial 80 patients is promising, the study may be expanded to potentially support accelerated approval. Preliminary top-line data from this study are anticipated in mid-2016.
- Karyopharm is actively enrolling patients in three later-stage clinical studies evaluating selinexor: one in older patients with relapsed/refractory AML (SOPRA study), the second in patients with relapsed/refractory DLBCL (SADAL study) and the third in patients with Richter's transformation (SIRRT study). Preliminary top-line data from all three studies are anticipated in the fourth quarter of 2016.
- Following evaluation of over 1,000 patients treated with selinexor to date, Karyopharm has determined that the recommended phase 2 dose (RP2D) for patients with the majority solid tumors and selected hematologic malignancies is 60 mg fixed dose, twice weekly; the maximum tolerated dose is ~120 mg. The recommended dose in multiple myeloma is 80 mg selinexor + 20 mg of dexamethasone together, twice weekly. Doses of up to 100 mg twice weekly will continue to be evaluated in certain indications.
- In July 2015, Karyopharm amended the SOPRA study, a Phase 2 randomized clinical trial of single-agent, oral selinexor in older patients with acute myeloid leukemia, or AML, to reduce the dose from 55mg/m^2 to a fixed dose of 60mg, which corresponds to approximately 35 mg/m^2. Dosing will remain twice weekly. This change was implemented based on ongoing safety and tolerability evaluations in the SOPRA study, as well as maturing data from AML patients in the Phase 1 first-in-human clinical trial of selinexor. The SOPRA study uses a two-to-one randomization of AML patients to selinexor or physician's choice and, therefore, approximately twice as many cases of sepsis would be expected on the selinexor arm compared with the physician's choice arm. As of the end of July 2015, there have been eight reports of sepsis in seven patients receiving selinexor 55 mg/m^2 on the SOPRA study, as compared with two reports of sepsis in two patients receiving physician's choice on that study. Therefore, although the numbers are small, and sepsis is often observed in patients with AML, the incidence of sepsis appears to be higher in the patients receiving selinexor. In addition, as our data are maturing, an apparent increase in the incidence of sepsis in patients with relapsed or refractory AML receiving high doses of selinexor twice weekly was noted in Karyopharm's Phase 1 clinical trial in hematologic malignancies. Importantly, doses of 60mg twice weekly do not appear to be associated with any increase in sepsis or other infection-related events in patients with hematologic malignancies or solid tumors. In addition, the majority of the patients with AML in the Phase 1 study who showed a response to selinexor treatment, including patients with complete remissions, received selinexor at doses of approximately 60mg or below. As a result of the change in dose, the SOPRA study will now have an interim assessment in mid-2016 with topline data expected in the fourth quarter of 2016.
- In July 2015, Karyopharm amended the protocol of SIRRT, a Phase 2 clinical study of single-agent, oral selinexor in patients with Richter's transformation, an aggressive form of lymphoma, to include patients with newly diagnosed Richter's transformation. There is no standard of care for patients with Richter's transformation and these patients have an extremely poor prognosis. As a result of these factors, and in order to improve patient accrual, in consultation with key opinion leaders in the area, Karyopharm determined that there was a compelling rationale to amend the SIRRT protocol to include patients who had not yet received chemotherapy to treat Richter's transformation. Karyopharm is now implementing the revised protocol across SIRRT study sites in the United States and Europe.

- Karyopharm expects to commence the STOMP ("**S**elinexor and Backbone **T**reatments **o**f Multiple **M**yeloma **P**atients") study in the third quarter with support from Myeloma Canada. In this multi-arm clinical study, Karyopharm plans to evaluate the combination of selinexor and low dose dexamethasone with backbone therapies including bortezomib, pomalidomide or lenalidomide in patients with multiple myeloma. Selinexor and low dose dexamethasone is already being combined with Kyprolis in an Investigator Sponsored Trial, where promising preliminary data were presented at ASH 2014.
- Karyopharm is currently conducting company-sponsored trials of single-agent selinexor in four solid tumor indications. At ASCO 2015, Karyopharm reported responses and disease control in patients with heavily pretreated gynecologic malignancies (SIGN study) and in recurrent glioblastoma multiforme (KING study); accrual to these studies is continuing. Karyopharm is also continuing to accrue patients to the SHIP study, a phase 2 study of selinexor in previously treated, hormone-refractory prostate cancer. The fourth phase 2 solid tumor study, the STARRS study, involves patients with relapsed or refractory squamous cell tumors. Enrollment to the head and neck cohort of this study has been completed and, due to very slow accrual in the lung and esophageal squamous carcinoma cohorts, Karyopharm is terminating further enrollment to these arms and finalizing the study. Additional trials with selinexor in combination with various chemotherapies are ongoing and may include patients with squamous cell carcinomas.
- In addition, a number of investigator-sponsored (ISTs) or company-sponsored clinical studies evaluating the potential of selinexor in combination with either chemotherapy or targeted agents are currently ongoing or planned.

Second Quarter June 30, 2015 Financial Results

Cash, cash equivalents and investments as of June 30, 2015, including restricted cash, totaled $256.0 million, compared to $285.3 million as of March 31, 2015.

For the quarter ended June 30, 2015, research and development expense was $27.0 million compared to $13.2 million for the quarter ended June 30, 2014. For the quarter ended June 30, 2015, general and administrative expense was $6.2 million compared to $3.3 million for the quarter ended June 30, 2014. The increase in research and development expenses resulted primarily from the increase in expenses related to the continued clinical development of selinexor. The increase in general and administrative expense resulted primarily from the costs of being a public company and an increase in stock-based compensation.

Karyopharm reported a net loss of $32.7 million, or $0.92 per share, for the quarter ended June 30, 2015, compared to a net loss of $16.4 million, or $0.55 per share, for the quarter ended June 30, 2014. Net loss includes stock-based compensation expense of $4.5 million and $3.9 million for the quarters ended June 30, 2015 and June 30, 2014, respectively.

Financial Outlook

Based on current operating plans, Karyopharm expects that its existing cash and cash equivalents will fund its research and development programs and operations into 2018, including moving the four later-stage clinical studies to their next data inflection points. Karyopharm expects to end 2015 with greater than $200 million in cash, cash equivalents and investments.

"Karyopharm continues to maintain a very strong balance sheet, with approximately $256M in cash as of the end of the second quarter of 2015," said Justin Renz, Executive Vice President, Chief Financial Officer & Treasurer. "As for financial guidance this year, we remain on track to end 2015 with greater than $200M in cash."

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 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 activity against a variety of different human cancers, SINE™ compounds have also shown biologica activity in models of cancer, inflammation, autoimmune disease, certain viruses, and wound-healing. Karyopharm was founded by Dr. Sharon Shacham and is located in Newton, Massachusetts. 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, including the timing of initiation of certain trials and of the reporting of data from such trials. Such statements are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from the company's current expectations. For example, there can be no guarantee that any of Karyopharm's SINE™ compounds, including selinexor (KPT-330) or any PAK4 inhibitor, or any other drug candidate that Karyopharm is developing 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; 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 June 30, 2015, which is on file with the Securities and Exchange Commission (SEC) as of August 10, 2015, 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 Karyopharm expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

Karyopharm Therapeutics Inc.

CONDENSED CONSOLIDATED BALANCE SHEETS

(unaudited)

(in thousands, except share and per share amounts)

	June 30, 2015	December 31, 2014
Assets		
Current assets:		
Cash and cash equivalents	$ 24,231	$ 150,609
Short-term investments	196,955	55,115
Prepaid expenses and other current assets	4,066	2,027
Total current assets	225,252	207,751
Property and equipment, net	3,234	2,754
Long-term investments	34,407	8,658
Other assets	—	774
Restricted cash	400	400
Total assets	$ 263,293	$ 220,337
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 4,469	$ 6,288
Accrued expenses	9,333	5,825
Deferred rent	200	126
Other current liabilities	97	62
Total current liabilities	14,099	12,301
Deferred rent, net of current portion	1,867	1,242
Total liabilities	15,966	13,543

Stockholders' equity:		
Preferred stock, $0.0001 par value; 5,000,000 shares authorized; none issued and outstanding	—	—
Common stock, $0.0001 par value; 100,000,000 shares authorized; 35,703,418 and 32,699,380 shares issued and outstanding at June 30, 2015 and December 31, 2014, respectively	4	3
Additional paid-in capital	444,574	345,166
Accumulated other comprehensive loss	(143)	(29)
Accumulated deficit	(197,108)	(138,346)
Total stockholders' equity	247,327	206,794
Total liabilities and stockholders' equity	$ 263,293	$ 220,337

Karyopharm Therapeutics Inc.

CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS

(unaudited)

(in thousands, except share and per share amounts)

	Three Months Ended, June 30,		Six Months Ended June 30,	
	2015	2014	2015	2014
Contract and grant revenue	$ 150	$ 21	$ 150	$ 193
Operating expenses:				
Research and development	27,006	13,159	47,757	24,138
General and administrative	6,157	3,310	11,556	6,214
Total operating expenses	33,163	16,469	59,313	30,352
Loss from operations	(33,013)	(16,448)	(59,163)	(30,159)
Other income:				
Interest income	267	17	408	34
Other income (expense)	51	—	(7)	—
Total other income, net	318	17	401	34
Net loss	$ (32,695)	$ (16,431)	$ (58,762)	$ (30,125)
Net loss per share applicable to common stockholders—basic and diluted	$ (0.92)	$ (0.55)	$ (1.65)	$ (1.02)
Weighted-average number of common shares outstanding used in net loss per share applicable to common stockholders—basic and diluted	35,697,012	29,659,457	35,508,146	29,633,215

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