Karyopharm to Present Updated SIGN Phase 2 Clinical Data at European Society of Medical Oncology 2016 Annual Meeting

- Single-Agent Selinexor Demonstrates Robust Clinical Benefit and Favorable Tolerability in Patients with Heavily Pre-treated Gynecologic Cancers -
- 49% Disease Control Rate Observed in Ovarian Cancer and 45% Observed in Endometrial Cancer —
- Compelling Biomarker Data for Selinexor in Gynecologic and Colorectal Cancers also Highlighted -

NEWTON, Mass., Oct. 05, 2016 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced that an oral presentation highlighting updated clinical data from the Company's ongoing Phase 2 study of selinexor (KPT-330), its lead, novel, oral Selective Inhibitor of Nuclear Export / SINE™ compound that inhibits exportin 1 (XPO1), for the treatment of gynecological cancers (the SIGN study) will be presented at the European Society of Medical Oncology (ESMO) 2016 annual meeting being held October 7-11, 2016 in Copenhagen, Denmark. Two posters featuring predictive biomarker data supporting selinexor's activity in gynecological and colorectal cancers will also be presented.

In the oral presentation, titled "Results of a Phase 2 Trial of Selinexor, an Oral Selective Inhibitor of Nuclear Export (SINE) in 114 Patients with Gynecological Cancers," Ignace B. Vergote, MD, PhD, Head of the Department of Gynecologic Oncology, Catholic University of Leuven, Belgium, and lead investigator of the SIGN study, will describe clinical data from the study, which includes durable anti-cancer activity in gynecological malignancies with disease control rates up to 49% and good tolerability.

"There is a significant need for new therapies for patients with progressive gynecological cancers," said Dr. Vergote. "We are excited by the anti-tumor activity observed in this study with single-agent oral selinexor, especially in heavily pre-treated patients with relapsed ovarian and endometrial cancers. Selinexor-associated adverse events were found to be manageable with supportive care and dose modifications as demonstrated by the number of patients who have remained on study after achieving disease control, with some continuing treatment for longer than 12 months. Notably, we found that ovarian cancer patients receiving 50 mg/m2 (approximately 80 mg) of selinexor once weekly achieved similar benefit with considerably fewer adverse events compared to those receiving twice weekly dosing. We look forward to further elucidating the potential of oral selinexor in late-stage clinical trials in ovarian and endometrial cancers."

"The increasing body of clinical data supporting the efficacy, safety and tolerability of single-agent selinexor for the treatment of gynecological cancers, especially the impressive disease control rates and partial responses observed in patients with ovarian and endometrial cancers, is very encouraging and clearly demonstrates the potential of this first-in-class oral agent," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "In addition to the SIGN clinical data, the biomarker data to be presented by our researchers and collaborators at ESMO this year continue to expand our understanding of the underlying biological mechanisms that drive selinexor's anti-cancer activity. Collectively, these data provide important insights that will help guide our future clinical development of selinexor not only in gynecologic and colorectal cancers, but across a wide variety of malignancies."

A summary of data from 102 evaluable patients treated in the SIGN study as of September 12, 2016 are outlined in the following table and described below. Twelve patients were non-evaluable for best response based on lack of tumor assessment (no PET-CT scans) after baseline.

Cancer Type	Dose	N	DCR (%)	PR (%)
Ovarian	35mg/m2 (BIW)	18	11 (61%)	2 (11%)
	50mg/m2 (BIW)	22	10 (45%)	3 (14%)
	50mg/m2 (QW)	19	8 (42%)	3 (16%)
	All Doses	59	29 (49%)	8 (14%)
Endometrial	50mg/m2 (BIW)	20	9 (45%)	3 (15%)
Cervical	50mg/m2 (BIW)	23	6 (26%)	1 (4%)

*Responses were adjudicated according to the Response Evaluation Criteria in Solid Tumors (RECIST v1.1) based on interim unaudited data. DCR=Disease Control Rate (complete response + partial response + stable disease for at least 12 weeks)

- Of the 59 evaluable patients with ovarian cancer, 29 met the primary endpoint (8 patients (14%) achieved a confirmed partial response (PR) and 21 patients achieved stable disease for at least 12 weeks (SD≥12 weeks)), for a disease control rate (DCR) of 49%. Median progression free survival (PFS) for the ovarian cancer arm was 3 months and median overall survival (OS) was 7 months.
- Of the 20 evaluable patients with endometrial cancer, 9 met the primary endpoint (3 confirmed PRs and 6 with SD≥12 weeks), for a DCR of 45%. Median PFS for the endometrial cancer arm was 3 months and median OS was 8 months.
- Across all arms, the most common grade 2 or 3 adverse events were fatigue, nausea, anemia, anorexia, vomiting, weight loss and thrombocytopenia, which were manageable with supportive care. Notably, grade 3 adverse events were significantly reduced in patients with ovarian cancer receiving once weekly dosing compared to twice weekly dosing. One incidence of grade 4 thrombocytopenia without bleeding was also reported.
- For the 44 patients who met the DCR criteria, the median time on study was 20 weeks. Fifteen patients remained on single-agent selinexor for greater than 6 months, including 4 patients continuing on treatment for greater than 12 months.

Selinexor Biomarker Data

Two posters featuring biomarker data supporting selinexor's activity in gynecological and colorectal cancers will also be presented:

- In Poster 1: "Circulating Tumor Cell Number Predicts Time to Progression (TTP) in Patients with Heavily Pretreated Gynecological Cancers Treated with Selinexor (SEL)," Karyopharm researchers demonstrate the feasibility and prognostic value of identifying and quantifying circulating tumor cells (CTCs) in the blood of patients with gynecological cancers (ovarian, endometrial and cervical). Based on patients from Karyopharm's Phase 2 SIGN study, the results of this biomarker study suggest that CTC count prior to selinexor treatment may correlate to the length of time a patient remains on study; patients with lower CTC counts at baseline remained on study longer than those with higher counts. Karyopharm believes this information could be useful in identifying patients with heavily pretreated gynecological cancers who may benefit from treatment with single-agent oral selinexor.

- In Poster 2: "RAS/AKT Pathway Mutations as Predictive Biomarkers in Patients with Colorectal Cancer Treated with the Exportin 1 (XPO1) Inhibitor Selinexor (SEL) — Inhibition of Nuclear-Cytoplasmic Translocation of p27 as a Mechanism of Anti-Tumour Activity," Karyopharm collaborator Dr. V.Y. Heong, National University Hospital, Singapore, describes data in which treatment with selinexor appears to lead to longer PFS in patients with advanced colorectal cancer (CRC) with RAS and/or AKT pathway mutations, compared to CRC patients without these mutations. By analyzing both pre- and post-selinexor treated CRC biopsy samples, the researchers confirmed increased nuclear retention of p27 in the RAS/AKT mutant tumors suggesting that p27 could be a key anti-tumor mechanism in RAS/AKT pathway activated CRC tumors. These data also suggest that selinexor could have enhanced activity against colorectal and other tumors with RAS mutations, which are generally difficult to treat with currently available agents.

More About the Phase 2 SIGN Study Design

The Phase 2 SIGN study is an open-label clinical trial evaluating the efficacy and safety of selinexor in patients with heavily pre-treated gynecological cancers including ovarian, endometrial and cervical cancer. Patients in the ovarian cancer arm receive oral selinexor at a dose of 35 or 50 mg/m2 twice weekly or 50 mg/m2 once weekly, while patients in the endometrial and cervical cancer arms receive oral selinexor at a dose of 50 mg/m2 twice weekly. The primary endpoint of the study is disease control rate (DCR, defined as complete responses (CRs), plus partial responses (PRs), plus stable disease for at least 12 weeks (SD≥12 weeks)) assessed according to RECIST (v1.1) criteria. A full description of the study is available at www.clinicaltrials.gov (NCT02025985).

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 1,700 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 combination with low-dose dexamethasone (STORM) and backbone therapies (STOMP), and in acute myeloid leukemia (SOPRA), diffuse large B-cell lymphoma (SADAL), and liposarcoma (SEAL), among others. Karyopharm plans to initiate a pivotal randomized Phase 3 study of selinexor in combination with bortezomib (Velcade®) and low-dose dexamethasone (BOSTON) in patients with multiple myeloma in early 2017. 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 the Company's clinical development priorities for selinexor. The latest 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, 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), 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 June 30, 2016, which was filed with the Securities and Exchange Commission (SEC) on August 4, 2016, 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.

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Contact:
Justin Renz
(617) 658-0574
jrenz@karyopharm.com

Gina Nugent
(617) 460-3579
nugentcomm@aol.com
