Karyopharm Reports Interim Phase 2b SADAL Data at the 2017 American Association for Cancer Research Annual Meeting

Selinexor Achieves Robust and Prolonged Response Rates in Patients with Relapsed or Refractory DLBCL, Including Against Both GCB and Non-GCB Subtypes
28.6% Overall Response Rate Demonstrated with a Median Duration of Greater than Seven Months
Top-Line Data from SADAL Study Expected in Mid-2018

NEWTON, Mass., April 04, 2017 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, announced that updated interim clinical data from its Phase 2b Selinexor Against Diffuse Aggressive Lymphoma (SADAL) study evaluating lead product candidate, selinexor (KPT-330), an oral Selective Inhibitor of Nuclear Export / SINE™ compound, in patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) was presented today in a late-breaking poster at the 2017 American Association for Cancer Research (AACR) annual meeting in Washington, DC. In the SADAL study, selinexor achieved a 28.6% overall response rate (ORR) in patients with relapsed or refractory DLBCL. Importantly, the responses were shown to be durable with a median duration of response (DOR) of greater than seven months, including prolonged complete responses (CRs).

"Data from the ongoing SADAL study demonstrate robust single-agent activity of selinexor and prolonged response rates in this heavily pretreated DLBCL patient population, including against both the GCB and non-GCB (ABC) subtypes," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "The observed response rates were consistent across both the 60mg and 100mg treatment arms, but greater durability and tolerability was observed in the 60mg arm. Based on these results and following agreement with FDA, a study amendment is underway to discontinue the 100mg treatment arm and focus solely on the 60mg treatment arm where we plan to add approximately 90 patients. We look forward to reporting top-line data from the SADAL study in mid-2018. Should the data confirm the current results, we plan to apply for accelerated approval for the treatment of relapsed / refractory DLBCL."

Updated Phase 2b SADAL Clinical Data in Relapsed or Refractory DLBCL

In a late-breaking poster presentation titled, "A Phase 2b randomized study of selinexor in patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) demonstrates durable responses in both GCB and non-GCB subtypes," Marie Maerevoet, MD of the Institute Jules Bordet in Belgium presented updated clinical data from the ongoing Phase 2b SADAL study.

A summary of the efficacy data as presented at AACR 2017 is outlined in the following table and described below.

Best Responses* in Patients as of 1 March 2017

Category	N	ORR (%)	DCR (%)	CR (%)	PR (%)	SD (%)	PD (%)	NE (%)
All patients	63	18 (28.6%)	27 (42.9%)	7 (11.1%)	11 (17.5%)	9 (14.3%)	29 (46.0%)	7 (11.1%)
60 mg	32	9 (28.1%)	12 (37.5%)	4 (12.5%)	5 (15.6%)	3 (9.4%)	17 (53.1%)	3 (9.4%)
100 mg	31	9 (29.0%)	15 (48.4%)	3 (9.7%)	6 (19.4%)	6 (19.4%)	12 (38.7%)	4 (12.9%)
GCB-Subtype	32	8 (25.0%)	14 (43.8%)	3 (9.4%)	5 (15.6%)	6 (18.8%)	13 (40.6%)	5 (15.6%)
Non-GCB-Subtype	31	10 (32.3%)	13 (41.9%)	4 (12.9%)	6 (19.4%)	3 (9.7%)	16 (51.6%)	2 (6.5%)

*Responses were adjudicated according to the Lugano Classification (Cheson, 2014) by an independent central radiological review committee. ORR=Overall Response Rate (CR+PR), CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease, DCR=Disease Control Rate (CR+PR+SD), NE=Not Evaluable for Response. Responses as of March 1, 2017 based on interim unaudited data.

Based on the intention-to-treat analysis of the first 63 patients (median of 3 prior treatment regimens (range 2-5)), as adjudicated by an independent central radiological committee, 18 patients responded (7 patients with a CR and 11 patients with a PR) for an ORR 28.6%. An additional 9 patients experienced SD, for a DCR of 42.9%. The median overall survival was 8 months for all patients, consistent with published data in this population. As of the data cutoff date, median survival for the responders had not been reached and is over 9 months. The median DOR across all patients was greater than 7 months and responses tended to occur rapidly with a median of 2 months to onset. Among patients who responded, the median time on treatment was 9 months with a follow up of 13 months. As of the data cutoff date, 9 patients who responded remained on treatment, including 6 patients with a CR.

Selinexor showed similar activity against GCB and non-GCB subtypes of DLBCL: Of the 32 patients with DLBCL of the GCB-subtype, 8 responded (3 patients with a CR, 5 patients with a PR and 6 patients with SD) for an ORR of 25.0% and DCR of 43.8%. Of the 31 patients with DLBCL of the non-GCB-subtype (ABC), 10 responded (4 patients with a CR, 6 patients with a PR and 3 patients with SD) for an ORR of 32.3% and DCR of 41.9%.

Among the 72 patients evaluated for safety, the most common adverse events (AEs) across both dosing groups were fatigue (65%), thrombocytopenia (54%), nausea (51%), anorexia (49%), vomiting (35%) and anemia (32%), and were primarily grades 1 and 2 and were managed with dose modifications and/or standard supportive care. As expected, the most common grade 3 and 4 AEs in the 60mg arm were thrombocytopenia (32%), neutropenia (16%), anemia (14%), and fatigue (11%) and were manageable with dose modifications and/or standard supportive care.

Dr. Maerevoet commented, "With the impressive and durable responses observed to date, including in both the GCB and non-GCB subtypes of DLBCL, single-agent selinexor is demonstrating the potential to become a new oral option for this difficult to treat patient population who are not candidates for transplantation and whose disease is unlikely to respond to further chemotherapy or targeted agents."

Planned Development Path for Selinexor in DLBCL

As a result of the interim data and in consultation with FDA, Karyopharm is amending the SADAL study protocol to become a single-arm study focusing solely on single-agent selinexor dosed at 60mg twice weekly, eliminating the 100mg arm. The study is also being amended to reduce the 14-week treatment-free period to 8 weeks in patients who achieved at least a PR on their most recent therapy. Patients who were refractory or did not achieve at least a PR on their prior therapy will continue with the 14-week treatment-free period. The FDA agreed

that the modification to a single-arm study was reasonable and that the proposed trial design and indication appear appropriate for accelerated approval, though eligibility for accelerated approval will depend on the complete trial results and available therapies at the time of regulatory action. The Company plans to enroll up to an additional 90 patients to the new 60mg single-arm cohort and expects to report top-line results from the SADAL study in mid-2018.

Title: A Phase 2b randomized study of selinexor in patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) demonstrates durable responses in both GCB and non-GCB subtypes
Presenter: Marie Maerevoet, Institute Jules Bordet
Poster Board #: 13
Session: Phase I-III Clinical Trials and Pediatric Clinical Trials
Location: Convention Center, Halls A-C, Poster Section 33
Date and Time: Tuesday, April 4, 2017 from 1:00 PM - 5:00 PM ET

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 1,900 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 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. 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, 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 Annual Report on Form 10-K for the year ended December 31, 2016, which was filed with the Securities and Exchange Commission (SEC) on March 16, 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 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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