Karyopharm Reports Positive Top-Line Phase 2b SADAL Data for Selinexor in Patients with Diffuse Large B-Cell Lymphoma at the American Society of Hematology 2018 Annual Meeting

December 1, 2018

-- 29.6% Overall Response Rate Including 9.6% Complete Response Rate --

-- Amongst the Patients with Complete or Partial Response, Median Duration of Response was 9.2 Months and Median Overall Survival was 29.7 months --

-- Company Plans to Submit New Drug Application to the FDA in the First Half of 2019 --

NEWTON, Mass, Dec. 01, 2018 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today reported positive top-line results from the Phase 2b SADAL (**S**elinexor **A**gainst **D**iffuse **A**ggressive **L**ymphoma) study evaluating selinexor, the Company's first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound, in patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after at least two prior multi-agent therapies and who are ineligible for transplantation, including high dose chemotherapy with stem cell rescue. The data were highlighted in a poster presentation at the American Society of Hematology (ASH) 2018 Annual Meeting in San Diego. For the SADAL study's primary endpoint, single-agent selinexor achieved a 29.6% overall response rate (ORR), which included a 9.6% complete response (CR) rate in patients with heavily pretreated relapsed or refractory DLBCL. Key secondary endpoints included a median duration of response (DOR, in the responding patients) of 9.2 months and median overall survival (OS, across the entire study) of 9.1 months.

Selinexor recently received Fast Track designation from the FDA for the patient population evaluated in the SADAL study. Karyopharm plans to submit a New Drug Application (NDA) to the FDA during the first half of 2019, with a request for accelerated approval for oral single-agent selinexor as a new treatment for patients with relapsed or refractory DLBCL.

Top-Line Phase 2b SADAL Results

Based on the modified intention-to-treat analysis from the first 115 of 127 patients (median of 2 prior treatment regimens with a range 1-6), as adjudicated by an independent central radiological committee, 34 patients responded (11 patients with a CR and 23 patients with a PR) for an ORR of 29.6%. An additional 8 patients experienced stable disease (SD) for a disease control rate of 36.5%. The median DOR across responding patients was 9.2 months and responses tended to occur rapidly. Patients with a CR had a median DOR of 23.0 months and patients with a PR had a median DOR of 7.8 months. As of the data cutoff date of November 15, 2018, 7 patients who achieved a CR remained on treatment. In addition, 12 patients remain on treatment, but as of November 15th, had not reached their first response assessment and are not included in the top-line efficacy analyses.

Among the patients evaluated for safety as of the data cutoff date, the most common treatment-related adverse events (AEs) were gastrointestinal and constitutional symptoms, along with cytopenias; most manageable with dose modifications and/or supportive care. The most common non-hematologic AEs were nausea (50.0%), fatigue (35.9%), and anorexia (32.0%) and mostly Grade 1 and 2 events. As expected, the most common Grade 3 and 4 AEs were thrombocytopenia (35.2%), neutropenia (20.3%), and anemia (10.9%) and were generally not associated with clinical sequelae. No significant major organ toxicities were observed, and bleeding and infection rates were low.

The median OS was 9.1 months for all patients in the study. As of the data cutoff date, median survival for the patients with a CR or PR was 29.7 months. The median survival for patients with best response of progressive disease or who were not evaluable for response was 3.2 months.

Selinexor showed robust, single-agent activity in patients with either GCB or non-GCB subtypes of DLBCL: of the 53 patients with the GCB-subtype, 18 responded (5 patients with a CR and 13 patients with a PR) for an ORR of 34.0%. Of the 57 patients with the non-GCB subtype, 12 responded (6 patients with a CR and 6 patients with a PR) for an ORR of 21.1%. In addition, there were 5 patients enrolled whose subtype was unclassified and 4 of these patients achieved a PR.

"The SADAL data presented at ASH this year demonstrate that oral selinexor, when administered as a single-agent, is clinically active and capable of producing durable responses associated with prolonged overall survival," said Marie Maerevoet, MD, Institute Jules Bordet, "The 60mg twice weekly oral dose continues to be well tolerated with a low incidence of Grade 3 or greater adverse events, which were often manageable with dose modifications and supportive care. We are highly encouraged by the results of this single agent study in patients with heavily pretreated DLBCL who have limited available treatment options."

Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm, said, "In addition to the compelling efficacy and safety data observed with single agent oral selinexor, we were especially pleased to see strong response rates in patients with both the GCB and non-GCB subtypes. This is especially important because the prognosis in patients with refractory disease and the GCB-subtype is particularly poor. We believe that if selinexor is ultimately approved for use in patients with DLBCL, it will provide a meaningful therapeutic option for patients battling refractory disease regardless of DLBCL subtype. We look forward to submitting these data to the FDA during the first half of 2019 as part of a New Drug Application, with a request for accelerated approval."

Details for the Poster Presentation at ASH 2018:

Title: Single Agent Oral Selinexor Demonstrates Deep and Durable Responses in Relapsed/Refractory Diffuse Large B-Cell Lymphoma (DLBCL) in Both GCB and Non-GCB Subtypes: The Phase 2b SADAL Study

Presenter: Marie Maerevoet, Institute Jules Bordet, Brussels, Belgium
Abstract Number/Publication ID: 1677
Session: 626. Aggressive Lymphoma (Diffuse Large B-Cell and Other Aggressive B-Cell Non-Hodgkin Lymphomas)—Results from Prospective Clinical Trials: Poster I
Date and Time: Saturday, December 1, 2018; 6:15-8:15 PM PT
Location: San Diego Convention Center, Hall GH

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. To date, over 2,800 patients have been treated with selinexor. In April and September 2018, Karyopharm reported positive data from the Phase 2b STORM study evaluating selinexor in combination with low-dose dexamethasone in patients with penta-refractory multiple myeloma. 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) 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 with penta-refractory multiple myeloma. The Company also plans to submit a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) in early 2019 with a request for conditional approval. 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 diffuse large B-cell lymphoma (SADAL), 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 and to 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 the data from the STORM study in patients with penta-refractory myeloma 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 September 30, 2018, which was filed with the Securities and Exchange Commission (SEC) on November 8, 2018, 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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