Karyopharm to Present Selinexor Phase 2/3 SEAL Data at the American Society of Clinical Oncology 2018 Annual Meeting

June 1, 2018

Treatment with Selinexor Prolongs Progression-Free Survival Compared to Placebo (5.5 months versus 2.7 months, respectively) in Patients with Liposarcoma

Additional Selinexor Data Posters from Investigator-Sponsored Trials Show Early Signals of Activity and Good Tolerability in Combination with Approved Anti-Cancer Agents in Soft Tissue Sarcoma and Acute Myeloid Leukemia, and Evidence of Combinability with Immunotherapy

NEWTON, Mass., June 01, 2018 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced that four posters will be presented at the American Society of Clinical Oncology (ASCO) 2018 Annual Meeting taking place June 1-5, 2018 in Chicago. Among the poster presentations will be clinical results from the Phase 2 portion of the Company's Phase 2/3 SEAL study evaluating selinexor, its lead, oral SINE compound, in patients with advanced unresectable dedifferentiated liposarcoma. The remaining posters will highlight data from ongoing investigator-sponsored trials evaluating selinexor in combination with approved anti-cancer agents in hematologic and solid tumor malignancies.

"In the Phase 2 portion of the SEAL study, patients treated with oral selinexor achieved progression-free survival (PFS) of 5.5 months, compared to 2.7 months for placebo-treated patients, an increase of 2.8 months," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "Dedifferentiated liposarcoma is particularly difficult to treat because it is resistant to both standard chemotherapy and radiation and there is a significant unmet need for therapies with a novel mechanism that can help these patients with few effective treatment options. The Phase 3 portion of the SEAL study is currently ongoing and we are anticipating top-line data by the end of 2019. Other selinexor data presented at ASCO from ongoing investigator-sponsored research continue to highlight early signs of clinical activity and good tolerability when selinexor is combined with approved agents in soft tissue sarcoma (STS) and acute myeloid leukemia (AML), and additional compelling evidence for selinexor's potential combinability with checkpoint inhibitors, in this case in AML."

Phase 2 Portion of the Phase 2/3 SEAL Study Evaluating Selinexor in Patients with Liposarcoma

In the poster presentation titled, "Phase 2 results of selinexor in advanced dedifferentiated (DDLS) liposarcoma (SEAL) study: A phase 2/3, randomized, double blind, placebo controlled cross-over study," (Abstract #11512) Mrinal Gounder, MD, Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College and lead investigator of the SEAL study, presented detailed clinical data from the successful Phase 2 portion of the randomized, double-blind, placebo-controlled Phase 2/3 SEAL study evaluating oral selinexor (60mg twice weekly) in 56 patients with previously treated, advanced unresectable dedifferentiated liposarcoma (median 2 prior regimens (range 1-9)). Patients on placebo with confirmed progressive disease are permitted to cross over to the selinexor treatment arm.

For the primary endpoint of PFS, oral selinexor showed superiority over placebo, achieving a median PFS of 5.5 months, compared to 2.7 months for placebo with a hazard ratio (HR) of 0.67, representing a 33% reduction in the risk of progression or death. PFS was assessed by Independent Central Radiological Review based on RECIST v1.1. Additional efficacy assessments included PFS by World Health Organization (WHO) response criteria. PFS per WHO criteria achieved a HR of 1.02. Oral selinexor demonstrated an expected and manageable safety profile, primarily with nausea, fatigue, anorexia and weight loss, with low levels of Grade 3/4 cytopenias, and no new or unexpected safety signals identified. The majority of treatment-related adverse events (AEs) were low grade and reversible with dose modifications and/or standard supportive care. These data from the Phase 2 portion of the SEAL study, which is now complete, demonstrate that treatment with selinexor improves PFS (RECIST v1.1) and supports the currently ongoing Phase 3 portion of the study using RECIST v1.1 response criteria [only], and for which top-line data are expected by the end of 2019.

Dr. Gounder stated, "Extending PFS in patients with recurrent, unresectable DDLS is an important clinical goal and these data highlight that oral selinexor continues to demonstrate an expected and manageable safety profile, along with the ability to prolong PFS. We are pleased to share these data with the medical community at ASCO this year and look forward to further elucidating selinexor's efficacy and safety in the already ongoing Phase 3 portion of the SEAL study."

Selinexor in Combination with Immunotherapy or Standard of Care Agents in Other Hematologic and Solid Tumor Malignancies

In the poster presentation titled, "Phase 1b study of selinexor, a first in class selective inhibitor of nuclear export (SINE) compound, in combination with doxorubicin in patients (pts) with locally advanced or metastatic soft tissue sarcoma (STS)," (Abstract #11562) Eoghan Ruadh Malone, MB BCh, BAO, BA, MSc, MRCPI, Princess Margaret Cancer Centre, presented results from an investigator-sponsored Phase 1b clinical study evaluating selinexor in combination with doxorubicin in 17 patients with locally advanced or metastatic STS. Disease subtypes included leiomyosarcoma (n=6), undifferentiated pleomorphic sarcoma (n=3), liposarcoma (n=2), malignant peripheral nerve sheath tumor (n=3) and other sarcomas (n=3). Preliminary data from this study show that the combination of selinexor plus doxorubicin has a manageable tolerability profile, along with early signals of anti-tumor activity, including partial responses (n=3). Median time on treatment is 20 weeks. Enrollment in the study is ongoing.

In the poster presentation titled, "Phase 1 study of selinexor plus mitoxantrone, etoposide, and cytarabine in acute myeloid leukemia," (Abstract #7048) Bhavana Bhatnagar, DO, Ohio State University Comprehensive Cancer Center, presented results from an investigator-sponsored Phase 1 clinical study evaluating selinexor in combination with mitoxantrone, etoposide and cytarabine (MEC) in patients with relapsed or refractory AML. Of the 23 evaluable patients, ten responded for an overall response rate of 44%, including six patients (26%) achieving complete remission (CR), two patients (9%) achieving CR with incomplete count recovery (CRi), and two patients (9%) achieving a morphologic leukemia-free state (MLFS). The tolerability of this combination regimen was similar to cytotoxic chemotherapy alone. The most common Grade ?3 adverse events were febrile neutropenia (48%), catheter related infection (26%), diarrhea (26%), hyponatremia (22%), sepsis (22%), fatigue (13%), hyperglycemia (13%), and hypotension (13%). The RP2D of selinexor in in this combination regimen was established to be 60mg twice weekly. Six responders proceeded to allogeneic stem cell transplantation without evidence of AML at the time of transplant.

In the poster presentation titled, "Profiling the immune checkpoint pathway in acute myeloid leukemia," (Abstract #7015) Paola Dama, PhD, University of Chicago, presented results from an investigator-sponsored study assessing the expression of immune checkpoint biomarkers in AML patients treated with the combination of selinexor, high-dose cytarabine (HiDAC) and mitoxantrone. Data from this study demonstrated high level expression of Gal9 in CD34- cells at diagnosis in patients who failed induction chemotherapy, compared to those in complete remission. There was no difference in PD-L1 expression between the two patient groups. Increased expression of Tim 3 on CD4 and CD8 T cells and high PD-1 in peripheral CD4+ T cell were observed at disease remission suggesting an exhausted

immune status at the time of disease remission on the selinexor + HiDAC + mitoxantrone combination, which the researchers believe could be targeted with the addition of checkpoint inhibitors.

Details for the ASCO 2018 selinexor presentations are as follows:

Company-sponsored Trials

Title: Phase 2 results of selinexor in advanced de-differentiated (DDLS) liposarcoma (SEAL) study: A phase 2/3, randomized, double blind, placebo controlled cross-over study
Lead author: Mrinal Gounder, Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College
Poster Board #: 257
Abstract #: 11512
Poster Discussion Session: Sarcoma
Poster Discussion Presenter: Mark Andrew Dickson
Date and Time: Saturday, June 2, 2018; 8:00 AM – 11:30 AM CT; Discussion from 3:18 - 3:30PM CT
Location: Hall A

Investigator-sponsored Trials

Title: Phase 1 study of selinexor plus mitoxantrone, etoposide, and cytarabine in acute myeloid leukemia
Lead author: Bhavana Bhatnagar, Ohio State University Comprehensive Cancer Center
Poster Board #: 108
Abstract: 7048
Poster Session: Hematologic Malignancies—Leukemia, Myelodysplastic Syndromes, and Allotransplant
Date and Time: Monday, June 4, 2018; 8:00 AM – 11:30 AM CT
Location: Hall A

Title: Phase 1b study of selinexor, a first in class selective inhibitor of nuclear export (SINE) compound, in combination with doxorubicin in patients (pts) with locally advanced or metastatic soft tissue sarcoma (STS)
Lead author: Eoghan Ruadh Malone, Princess Margaret Cancer Centre
Poster Board #: 307
Abstract: 11562
Poster Session: Sarcoma
Date and Time: Saturday, June 2, 2018; 8:00 AM – 11:30 AM CT
Location: Hall A

Title: Profiling the immune checkpoint pathway in acute myeloid leukemia
Lead author: Paola Dama, University of Chicago
Poster Board #: 75
Abstract: 7015
Poster Discussion Session: Hematologic Malignancies – Leukemia, Myelodysplastic Syndromes, and Allotransplant
Date and Time: Monday, June 4, 2018; 8:00 AM – 11:30 AM CT; Discussion from 11:30 AM – 12:45 PM CT
Location: Hall A

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 2,400 patients have been treated with selinexor. In April 2018, Karyopharm reported positive top-line 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 plans to submit a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) during the second half of 2018, with a request for accelerated approval for oral selinexor as a 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) and as a potential backbone therapy in combination with approved therapies (STOMP), and 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 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 timing of submissions to regulatory authorities and the potential availability of accelerated approval pathways, the therapeutic potential of and potential clinical development plans for Karyopharm's drug candidates, especially selinexor. 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 drug candidates, including selinexor, will successfully complete necessary clinical development phases, that development of any of Karyopharm's drug candidates will continue or that any feedback from regulatory authorities will ultimately lead to the approval of selinexor or any of Karyopharm’s other drug candidates. 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 March 31, 2018, which was filed with the Securities and Exchange Commission (SEC) on May 10, 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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