Karyopharm Announces Presentation of New XPOVIO® (Selinexor) Data in Patients with Acute Myeloid Leukemia at the American Society of Hematology 2020 Annual Meeting

-- In a Randomized Investigator Sponsored Study, XPOVIO in Combination with Standard Induction and Consolidation Chemotherapy Demonstrated Improved Survival in Older, Fit Patients with Acute Myeloid Leukemia -
-- Company to Host Virtual Investor and Analyst Event on Tuesday, December 8th at 1:00 PM ET to Review Highlights from the Data Presented at ASH 2020 --

NEWTON, Mass., Dec. 7, 2020 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced an oral presentation highlighting data related to XPOVIO® (selinexor), the Company's first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound, was presented at the American Society of Hematology (ASH) 2020 Annual Meeting taking place virtually December 5-8, 2020. The presentation featured new data from a randomized, investigator-sponsored Phase 2 study evaluating combination chemotherapy with or without XPOVIO in newly diagnosed older adults with acute myeloid leukemia (AML).

"AML is an aggressive form of blood cancer that begins in the bone marrow and is frequently characterized by resistance to currently available therapies, especially in elderly patients," said Timothy S. Pardee, M.D., Ph.D., Associate Professor, Hematology and Oncology, Wake Forest School of Medicine and lead author of the presentation. "The data presented today at ASH 2020, show that XPOVIO in combination with standard induction and consolidation chemotherapy appears highly active in older patients with de novo AML. Despite the small size of the study, XPOVIO in combination was associated with a significant survival improvement and a higher overall response rate than standard chemotherapy alone. In addition, accompanying preclinical work suggests that XPOVIO may increase response to cytarabine, one of the standard chemotherapy drugs used to treat AML, by interfering with nuclear-mitochondrial communication. As novel approaches to treating patients with AML are desperately needed, we look forward to further evaluating this active regimen."

"AML is the most common form of acute leukemia in adults and unfortunately, very little improvement has been made in recent years in terms of improving long-term patient outcomes," said Sharon Shacham, PhD, MBA, Founder, President and Chief Scientific Officer of Karyopharm. "We are extremely pleased to see such striking results from the combination of XPOVIO and standard chemotherapy in newly diagnosed older patients with AML. We believe the data presented at ASH 2020 may encourage interest from the cancer research community to further evaluate the potential use of XPOVIO as a combination drug partner with other standard treatments in older patients with AML."

New Data from Phase 2 Study of XPOVIO in Combination with Chemotherapy in Older Patients with AML

In this randomized Phase 2 study, researchers evaluated standard intensive chemotherapy (the "7+3" regimen because it consists of cytarabine continuously for seven days, along with short infusions of an anthracycline drug on each of the first three days) with or without XPOVIO in newly diagnosed patients with AML who were 60 years of age or older. Responding patients could go on to receive high dose cytarabine consolidation therapy with or without XPOVIO as per initial randomization. Patients in the XPOVIO arm who completed all consolidation could then move to maintenance therapy with XPOVIO alone. Induction therapy consisted of cytarabine (by continuous infusion for seven days) and daunorubicin (on days 1-3). Consolidation consisted of cytarabine therapy. XPOVIO was dosed orally at 60mg twice weekly during induction and consolidation and once weekly during maintenance.

The following table is a summary of the efficacy results:

Cohort	All (n=28)	Standard Arm (n=7)	XPOVIO Arm (n=21)
Median overall survival (days)		265	839
Median progression-free survival (days)		108	558
Residual disease on nadir marrow	19% (5/27)	50% (3/6)	10% (2/21)

Complete remission (CR)	68% (19/28)	43% (3/7)	76% (16/21)
MRD negative CR	81% (13/16)	n/a	81% (13/16)
Overall response (CR+CRi)	75% (21/28)	43% (3/7)	86% (18/21)
No CR/CRi	26% (7/28)	57% (4/7)	14% (3/21)
Went on to transplant	29% (8/28)	14% (1/7)	33% (7/21)
Relapsed after CR	24% (5/21)	33% (1/3)	22% (4/18)

Key: CR=complete remission; CRi=complete remission with incomplete count recovery)

Diarrhea was the most common treatment-related adverse event (AE), resulting in dose modifications and dose holding. Additionally, seven patients (33%) on the XPOVIO arm experienced prolonged thrombocytopenia. Sixty-day mortality was 10% (2/21) of patients on the XPOVIO arm compared to 14% (1/7) of patients on the standard of care arm.

These results suggest that a 7+3 regimen in combination with XPOVIO has a manageable safety profile and is highly active in patients aged 60 and older. XPOVIO provided a statistically significant survival benefit (839 days versus 265 days; p=0.0472) in this small, randomized trial; ORR was also significantly improved on the XPOVIO arm.

In addition to the Phase 2 clinical research, preclinical studies were also conducted with murine AML cell lines to assess the mechanisms of chemo-sensitization. The results of this preclinical research showed that XPOVIO induces retention of topoisomerase II in the nucleus increasing sensitivity to anthracyclines (which block topoisomerase II), and significantly sensitizes cell lines to cytarabine. Existing research shows that AML cells increase mitochondrial oxygen consumption in response to cytarabine, which in turn leads to resistance. The ability of XPOVIO to interfere with this response was assessed. When co-treated with both cytarabine and XPOVIO, the treated AML cells showed a diminished mitochondrial oxygen response.

Details for the ASH 2020 presentations are as follows:

Title: Frontline selinexor and chemotherapy is highly active in older adults with Acute Myeloid Leukemia (AML)
Presenter: Timothy Pardee, Wake Forest School of Medicine
Abstract #: 633
Session: 615. Acute Myeloid Leukemia: Commercially Available Therapy, excluding Transplantation: Commercially Available Therapy, excluding Transplantation II
Date and Time: Monday, December 7, 2020, 11:45 a.m. ET
Location: Channel 12 (Virtual Meeting)

A PDF copy of this presentation are available **here.**

Virtual Investor and Analyst Event Conference Call and Webcast

Karyopharm will host a conference call and on Tuesday, December 8, 2020, at 1:00 p.m. Eastern Time, to review highlights from the ASH 2020 data presentations. The event will feature recognized myeloma and leukemia experts James Berenson, MD, Founder, President and Medical and Scientific Director of the Institute for Myeloma and Bone Cancer Research, and Dr. Timothy Pardee, MD, PhD, FACP, Wake Forest School of Medicine, along with members of the Karyopharm executive leadership team. To access the event, please dial (877) 870-4263 (local) or (412) 317-0790 (international) at least 10 minutes prior to the start time and ask to be joined into the Karyopharm Therapeutics call. A live audio webcast of the call will be available under "Events & Presentations" in the Investor section of the Company's website, http://investors.karyopharm.com/events-presentations. An archived webcast will be available on the Company's website approximately two hours after the event.

About XPOVIO® (selinexor)

XPOVIO is a first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound. XPOVIO functions by selectively binding to and inhibiting the nuclear export protein exportin 1 (XPO1, also called CRM1). XPOVIO blocks the nuclear export of tumor suppressor, growth regulatory and anti-inflammatory proteins, leading to accumulation of these proteins in the nucleus and enhancing their anti-cancer activity in the cell. The forced nuclear retention of these proteins can counteract a multitude of the oncogenic pathways that, unchecked, allow cancer cells with severe DNA damage to continue to grow and divide in an unrestrained fashion. Karyopharm received accelerated U.S. Food and Drug Administration (FDA) approval of XPOVIO in July 2019 in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody. Karyopharm has also submitted a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) with a request for conditional approval of selinexor in this same RRMM indication. Karyopharm's

supplemental New Drug Application (sNDA) requesting an expansion of its current indication to include the treatment for patients with multiple myeloma after at least one prior line of therapy has been accepted for filing by the FDA. In June 2020, Karyopharm received accelerated FDA approval of XPOVIO for its second indication in adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy. Selinexor is also being evaluated in several other mid-and later-phase clinical trials across multiple cancer indications, including as a potential backbone therapy in combination with approved myeloma therapies (STOMP), in liposarcoma (SEAL) and 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.

For more information about Karyopharm's products or clinical trials, please contact the Medical Information department at:

Tel: +1 (888) 209-9326
Email: medicalinformation@karyopharm.com

IMPORTANT SAFETY INFORMATION

Thrombocytopenia: XPOVIO can cause life-threatening thrombocytopenia, potentially leading to hemorrhage. Thrombocytopenia was reported in patients with multiple myeloma (MM) and developed or worsened in patients with DLBCL.

Thrombocytopenia is the leading cause of dosage modifications. Monitor platelet counts at baseline and throughout treatment. Monitor more frequently during the first 3 months of treatment. Institute platelet transfusion and/or other treatments as clinically indicated. Monitor patients for signs and symptoms of bleeding and evaluate promptly. Interrupt, reduce dose, or permanently discontinue based on severity of adverse reaction.

Neutropenia: XPOVIO can cause life-threatening neutropenia, potentially increasing the risk of infection. Neutropenia and febrile neutropenia occurred in patients with MM and in patients with DLBCL.

Obtain white blood cell counts with differential at baseline and throughout treatment. Monitor more frequently during the first 3 months of treatment. Monitor patients for signs and symptoms of concomitant infection and evaluate promptly. Consider supportive measures, including antimicrobials and growth factors (e.g., G-CSF). Interrupt, reduce dose, or permanently discontinue based on severity of adverse reaction (AR).

Gastrointestinal Toxicity: XPOVIO can cause severe gastrointestinal toxicities in patients with MM and DLBCL.

Nausea/Vomiting: Provide prophylactic antiemetics. Administer 5-HT3 receptor antagonists and other anti-nausea agents prior to and during treatment with XPOVIO. Interrupt, reduce dose, or permanently discontinue based on severity of ARs. Administer intravenous fluids to prevent dehydration and replace electrolytes as clinically indicated.

Diarrhea: Interrupt, reduce dose, or permanently discontinue based on severity of ARs. Provide standard anti-diarrheal agents, administer intravenous fluids to prevent dehydration, and replace electrolytes as clinically indicated.

Anorexia/Weight Loss: Monitor weight, nutritional status, and volume status at baseline and throughout treatment. Monitor more frequently during the first 3 months of treatment. Interrupt, reduce dose, or permanently discontinue based on severity of ARs. Provide nutritional support, fluids, and electrolyte repletion as clinically indicated.

Hyponatremia: XPOVIO can cause severe or life-threatening hyponatremia. Hyponatremia developed in patients with MM and in patients with DLBCL.

Monitor sodium level at baseline and throughout treatment. Monitor more frequently during the first 2 months of treatment. Correct sodium levels for concurrent hyperglycemia (serum glucose >150 mg/dL) and high serum paraprotein levels. Assess hydration status and manage hyponatremia per clinical guidelines, including intravenous saline and/or salt tablets as appropriate and dietary review. Interrupt, reduce dose, or permanently discontinue based on severity of the AR.

Serious Infection: XPOVIO can cause serious and fatal infections. Most infections were not associated with Grade 3 or higher neutropenia. Atypical infections reported after taking XPOVIO include, but are not limited to,

fungal pneumonia and herpesvirus infection.

Monitor for signs and symptoms of infection, and evaluate and treat promptly.

Neurological Toxicity: XPOVIO can cause life-threatening neurological toxicities.

Coadministration of XPOVIO with other products that cause dizziness or mental status changes may increase the risk of neurological toxicity.

Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, until the neurological toxicity fully resolves. Optimize hydration status, hemoglobin level, and concomitant medications to avoid exacerbating dizziness or mental status changes. Institute fall precautions as appropriate.

Embryo-Fetal Toxicity: XPOVIO can cause fetal harm when administered to a pregnant woman.

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with a female partner of reproductive potential to use effective contraception during treatment with XPOVIO and for 1 week after the last dose.

ADVERSE REACTIONS

The most common adverse reactions in ≥20% of patients with MM are thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea, and upper respiratory tract infection.

The most common ARs, excluding laboratory abnormalities, in ≥20% of patients with DLBCL are fatigue, nausea, diarrhea, appetite decrease, weight decrease, constipation, vomiting, and pyrexia. Grade 3-4 laboratory abnormalities in ≥15% of patients included thrombocytopenia, lymphopenia, neutropenia, anemia, and hyponatremia. Grade 4 laboratory abnormalities in ≥5% were thrombocytopenia, lymphopenia, and neutropenia.

In patients with MM, fatal ARs occurred in 9% of patients. Serious ARs occurred in 58% of patients. Treatment discontinuation rate due to ARs was 27%. The most frequent ARs requiring permanent discontinuation in ≥4% of patients included fatigue, nausea, and thrombocytopenia.

In patients with DLBCL, fatal ARs occurred in 3.7% of patients within 30 days, and 5% of patients within 60 days of last treatment; the most frequent fatal AR was infection (4.5% of patients). Serious ARs occurred in 46% of patients; the most frequent serious AR was infection. Discontinuation due to ARs occurred in 17% of patients.

USE IN SPECIFIC POPULATIONS

In MM, no overall difference in effectiveness of XPOVIO was observed in patients >65 years old when compared with younger patients. Patients ≥75 years old had a higher incidence of discontinuation due to an AR than younger patients, a higher incidence of serious ARs, and a higher incidence of fatal ARs.

Clinical studies in patients with relapsed or refractory DLBCL did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients.

The effect of end-stage renal disease (CLCR <15 mL/min) or hemodialysis on XPOVIO pharmacokinetics is unknown.

Please see full Prescribing Information.

To report SUSPECTED ADVERSE REACTIONS, contact Karyopharm Therapeutics Inc. at 1-888-209-9326 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

About Karyopharm Therapeutics

Karyopharm Therapeutics Inc. (Nasdaq: KPTI) is a commercial-stage pharmaceutical company pioneering novel cancer therapies and dedicated to the discovery, development, and commercialization of novel first-in-class drugs directed against nuclear export and related targets for the treatment of cancer and other major diseases. Karyopharm's Selective Inhibitor of Nuclear Export (SINE) compounds function by binding with and inhibiting the nuclear export protein XPO1 (or CRM1). Karyopharm's lead compound, XPOVIO® (selinexor), received accelerated approval from the U.S. Food and Drug Administration (FDA) in July 2019 in combination with dexamethasone as a treatment for patients with heavily pretreated multiple myeloma. In June 2020, XPOVIO was approved by the FDA as a treatment for patients with relapsed or refractory diffuse large B-cell lymphoma.

A Marketing Authorization Application for selinexor for patients with heavily pretreated multiple myeloma is also currently under review by the European Medicines Agency. 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 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 Karyopharm's expectations and plans relating to XPOVIO for the treatment of patients with AML; commercialization of XPOVIO or any of its drug candidates and the commercial performance of XPOVIO; submissions to, and the review and potential approval of selinexor by, regulatory authorities, including the Company's regulatory strategy, the anticipated availability of data to support such submissions, timing of such submissions and actions by regulatory authorities and the potential availability of accelerated approval pathways; the expected design of the Company's clinical trials; and 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, 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 Karyopharm will successfully commercialize XPOVIO; that regulators will agree that selinexor qualifies for conditional approval in the E.U. as a result of data from the STORM study or confirmatory approval in the U.S. or E.U. based on the BOSTON study in patients with multiple myeloma; 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 the development or commercialization of 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: the risk that the COVID-19 pandemic could disrupt Karyopharm's business more severely than it currently anticipates, including by negatively impacting sales of XPOVIO, interrupting or delaying research and development efforts, impacting the ability to procure sufficient supply for the development and commercialization of selinexor or other product candidates, delaying ongoing or planned clinical trials, impeding the execution of business plans, planned regulatory milestones and timelines, or inconveniencing patients; the adoption of XPOVIO in the commercial marketplace, the timing and costs involved in commercializing XPOVIO or any of Karyopharm's drug candidates that receive regulatory approval; the ability to retain regulatory approval of XPOVIO or any of Karyopharm's drug candidates that receive regulatory approval; 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; the ability of Karyopharm or its third party collaborators or successors in interest to fully perform their respective obligations under the applicable agreement and the potential future financial implications of such agreement; 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 indications 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, 2020, which was filed with the Securities and Exchange Commission (SEC) on November 2, 2020, 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.

SOURCE Karyopharm Therapeutics Inc.

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