



Karyopharm Presents XPOVIO® (selinexor) and Eltanexor Data at the European Hematology Association 2020 Virtual Annual Meeting

June 12, 2020

-- Selinexor Demonstrates a Significant Survival Benefit in Patients with Relapsed or Refractory DLBCL and Durable Responses in Important DLBCL Patient Subgroups, Including Those with Primary Refractory Disease and Regardless of Number of Prior Therapies --

NEWTON, Mass., June 12, 2020 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), an innovation-driven pharmaceutical company, today announced that eight posters relating to XPOVIO® (selinexor), the Company's first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound, and eltanexor, its next generation SINE compound, will be presented at the European Hematology Association (EHA) 2020 Virtual Annual Meeting taking place June 11-21, 2020.

The six selinexor abstracts include: (i) overall survival data from the Phase 2b SADAL study evaluating selinexor in patients with relapsed or refractory diffuse large-B-cell lymphoma (DLBCL) demonstrating a 9-month median overall survival in a patient population in which survival is expected to be <6 months based on several historical controls, with the median overall survival not yet reached in the 29% of patients who had partial or complete responses on single agent selinexor; (ii) a post-hoc analysis from the SADAL study demonstrating clinically meaningful response rates in the subgroup of patients with primary refractory DLBCL and treated with at least two prior regimens; (iii) a post-hoc analysis from the SADAL study demonstrating durable response rates regardless of the number of prior lines of therapy or prior treatment with high dose chemotherapy with autologous stem cell transplant; (iv) an assessment of molecular markers that may predict response to selinexor in patients with DLBCL; (v) data demonstrating the anti-myeloma effects of selinexor in combination with eukaryotic translation initiation factor 4E (eIF4E); and (vi) data demonstrating selinexor's potential to treat patients with acute myeloid leukemia harboring IDH2 pR172K mutations.

The two eltanexor abstracts include: (i) data demonstrating the efficacy of eltanexor in preclinical models of NPM1-mutated acute myeloid leukemia; and (ii) an assessment of molecular markers that may predict a response to eltanexor in patients with relapsed or refractory multiple myeloma.

"The Phase 2b SADAL study in patients with heavily pretreated DLBCL continues to generate encouraging efficacy and safety data from multiple datasets and post-hoc analyses, including a superior survival benefit over what has historically been observed with other therapies," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "As we await the decision from the U.S. Food and Drug Administration on our supplemental new drug application expected later this month, our sales force is actively preparing for the potential launch of XPOVIO in the additional indication of relapsed or refractory DLBCL. The SADAL data presented at EHA this year will be an important component of our physician education effort surrounding XPOVIO to treat patients with DLBCL, if approved."

Details for the EHA 2020 virtual poster presentations are as follows:

Selinexor

Title: Survival Among Patients with Relapsed/Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL) Treated with Single Agent Selinexor in the SADAL Study

Lead author: Marie Maerevoet, Institut Jules Bordet

Abstract #: EP1260

Session: 19. Aggressive Non-Hodgkin Lymphoma – Clinical

Title: Efficacy and Safety of Single Agent Oral Selinexor in Patients with Primary Refractory Diffuse Large B-Cell Lymphoma (DLBCL): A Post-Hoc Analysis of the SADAL Study

Lead author: Josee Zijlstra, Amsterdam Universitair Medische Centra, Vrije Universiteit, Cancer Center

Abstract #: EP1226

Session: 19. Aggressive Non-Hodgkin lymphoma – Clinical

Title: Effect of Prior Therapy on the Efficacy and Safety Of Oral Selinexor in Patients With Relapsed/Refractory (R/R) Diffuse Large B-cell Lymphoma (DLBCL): A Post-hoc Analysis of the SADAL Study

Lead author: George Follows, Addenbrooke's Hospital, Cambridge, United Kingdom

Abstract #: EP1244

Session: 19. Aggressive Non-Hodgkin lymphoma - Clinical

Title: Combined Inhibition of XPO1 and eIF4E Prevents Protein Translation resulting in Synergistic Anti-Myeloma Effects

Lead author: Shirong Li, Columbia University

Abstract #: EP1910

Session: 13. Myeloma and other monoclonal gammopathies – Biology & Translational Research

Title: IDH2 p.R172K Mutations in Patients with Acute Myeloid Leukemia (AML) May Be Associated with Favorable Response to Selinexor Treatment

Lead author: Christopher Walker, Karyopharm Therapeutics Inc.

Abstract #: EP484

Session: 03. Acute myeloid leukemia - Biology & Translational Research

Title: Comprehensive Assessment of Molecular Markers of Selinexor Response in Patients with Diffuse Large B-cell Lymphoma (DLBCL)

Lead author: Christopher Walker, Karyopharm Therapeutics Inc.

Abstract #: EP1328

Session: 20. Lymphoma Biology & Translational Research

Eltanexor

Title: Continuous XPO1 Inhibition with Eltanexor is Highly Effective in NPM1-mutated AML *In Vivo*

Lead author: Giulia Pianigiani, University of Perugia

Abstract #: EP441

Session: 03. Acute myeloid leukemia - Biology & Translational Research

Title: RNA and DNA Sequencing Reveal Markers of Response to the XPO1 Inhibitor Eltanexor in Patients with Relapsed or Refractory Multiple Myeloma (RRMM)

Lead author: Christopher Walker, Karyopharm Therapeutics Inc.

Abstract #: EP890

Session: 13. Myeloma and other monoclonal gammopathies - Biology & Translational Research

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 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. A supplemental New Drug Application was accepted by the FDA seeking accelerated approval for selinexor as a new treatment for patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), and selinexor has received Fast Track and Orphan designation and Priority Review from the FDA with a scheduled PDUFA date of June 23, 2020 for this patient population. 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), for which Karyopharm announced positive top-line results in March 2020. In May 2020, Karyopharm submitted a supplemental New Drug Application based on data from the Phase 3 BOSTON study. Additional, ongoing trials for selinexor include 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:

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IMPORTANT SAFETY INFORMATION

Thrombocytopenia

XPOVIO can cause thrombocytopenia, leading to potentially fatal hemorrhage. Thrombocytopenia was reported as an adverse reaction in 74% of patients, and severe (Grade 3-4) thrombocytopenia occurred in 61% of patients treated with XPOVIO. The median time to onset of the first event was 22 days. Bleeding occurred in 23% of patients with thrombocytopenia, clinically significant bleeding occurred in 5% of patients with thrombocytopenia and fatal hemorrhage occurred in <1% of patients.

Monitor platelet counts at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two 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 and/or reduce dose, or permanently discontinue based on severity of adverse reaction.

Neutropenia

XPOVIO can cause neutropenia, potentially increasing the risk of infection. Neutropenia was reported as an adverse reaction in 34% of patients, and severe (Grade 3-4) neutropenia occurred in 21% of patients treated with XPOVIO. The median time to onset of the first event was 25 days. Febrile neutropenia was reported in 3% of patients.

Obtain neutrophil counts at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two months of treatment. Monitor patients for signs and symptoms of concomitant infection and evaluate promptly. Consider supportive measures including antimicrobials for signs of infection and use of growth factors (e.g., G-CSF). Interrupt and/or reduce dose, or permanently discontinue based on severity of adverse reaction.

Gastrointestinal Toxicity

Gastrointestinal toxicities occurred in patients treated with XPOVIO.

Nausea/Vomiting

Nausea was reported as an adverse reaction in 72% of patients, and Grade 3 nausea occurred in 9% of patients treated with XPOVIO. The median

time to onset of the first nausea event was 3 days.

Vomiting was reported in 41% of patients, and Grade 3 vomiting occurred in 4% of patients treated with XPOVIO. The median time to onset of the first vomiting event was 5 days.

Provide prophylactic 5-HT₃ antagonists and/or other anti-nausea agents, prior to and during treatment with XPOVIO. Manage nausea/vomiting by dose interruption, reduction, and/or discontinuation. Administer intravenous fluids and replace electrolytes to prevent dehydration in patients at risk. Use additional anti-nausea medications as clinically indicated.

Diarrhea

Diarrhea was reported as an adverse reaction in 44% of patients, and Grade 3 diarrhea occurred in 6% of patients treated with XPOVIO. The median time to onset of diarrhea was 15 days.

Manage diarrhea by dose modifications and/or standard anti-diarrheal agents; administer intravenous fluids to prevent dehydration in patients at risk.

Anorexia/Weight Loss

Anorexia was reported as an adverse reaction in 53% of patients, and Grade 3 anorexia occurred in 5% of patients treated with XPOVIO. The median time to onset of anorexia was 8 days.

Weight loss was reported as an adverse reaction in 47% of patients, and Grade 3 weight loss occurred in 1% of patients treated with XPOVIO. The median time to onset of weight loss was 15 days.

Monitor patient weight at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two months of treatment. Manage anorexia and weight loss with dose modifications, appetite stimulants, and nutritional support.

Hyponatremia

XPOVIO can cause hyponatremia; 39% of patients treated with XPOVIO experienced hyponatremia, 22% of patients experienced Grade 3 or 4 hyponatremia. The median time to onset of the first event was 8 days.

Monitor sodium level at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two months of treatment. Correct sodium levels for concurrent hyperglycemia (serum glucose >150 mg/dL) and high serum paraprotein levels. Treat hyponatremia per clinical guidelines (intravenous saline and/or salt tablets), including dietary review. Interrupt and/or reduce dose, or permanently discontinue based on severity of adverse reaction.

Infections

In patients receiving XPOVIO, 52% of patients experienced any grade of infection. Upper respiratory tract infection of any grade occurred in 21%, pneumonia in 13%, and sepsis in 6% of patients. Grade ≥ 3 infections were reported in 25% of patients, and deaths resulting from an infection occurred in 4% of patients. The most commonly reported Grade ≥ 3 infections were pneumonia in 9% of patients, followed by sepsis in 6%. The median time to onset was 54 days for pneumonia and 42 days for sepsis. Most infections were not associated with neutropenia and were caused by non-opportunistic organisms.

Neurological Toxicity

Neurological toxicities occurred in patients treated with XPOVIO.

Neurological adverse reactions including dizziness, syncope, depressed level of consciousness, and mental status changes (including delirium and confusional state) occurred in 30% of patients, and severe events (Grade 3-4) occurred in 9% of patients treated with XPOVIO. Median time to the first event was 15 days.

Optimize hydration status, hemoglobin level, and concomitant medications to avoid exacerbating dizziness or mental status changes.

Embryo-Fetal Toxicity

Based on data from animal studies and its mechanism of action, XPOVIO can cause fetal harm when administered to a pregnant woman. Selinexor administration to pregnant animals during organogenesis resulted in structural abnormalities and alterations to growth at exposures below those occurring clinically at the recommended dose.

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 (incidence $\geq 20\%$) are thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea, and upper respiratory tract infection.

The treatment discontinuation rate due to adverse reactions was 27%; 53% of patients had a reduction in the XPOVIO dose, and 65.3% had the dose of XPOVIO interrupted. The most frequent adverse reactions requiring permanent discontinuation in 4% or greater of patients who received XPOVIO included fatigue, nausea, and thrombocytopenia. The rate of fatal adverse reactions was 8.9%.

Please see XPOVIO Full Prescribing Information available at www.XPOVIO.com.

About Eltanexor (KPT-8602)

Eltanexor (KPT-8602) is a second generation oral SINE compound, which is currently being investigated in clinical trials. Eltanexor functions by binding to and inhibiting the nuclear export protein XPO1 (also called CRM1), leading to the accumulation of tumor suppressor proteins in the cell nucleus. Eltanexor has demonstrated minimal brain penetration in animals, which has been associated with reduced toxicities in preclinical studies

while maintaining potent anti-tumor effects.

About Karyopharm Therapeutics

Karyopharm Therapeutics Inc. (Nasdaq: KPTI) is an innovation-driven pharmaceutical company 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 May 2020, Karyopharm submitted a supplemental New Drug Application requesting approval for XPOVIO as a new treatment for patients with multiple myeloma after at least one prior line of therapy based on the data from the Phase 3 BOSTON study. A Marketing Authorization Application for selinexor is also currently under review by the European Medicines Agency. A supplemental New Drug Application was also accepted by the FDA seeking accelerated approval for selinexor as a new treatment for adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL). 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 beliefs regarding selinexor's and eltanexor's ability to treat patients with relapsed or refractory diffuse large B-cell lymphoma, multiple myeloma, acute myeloid leukemia and other diseases and expectations related to potential regulatory submissions. 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 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 reducing 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 March 31, 2020, which was filed with the Securities and Exchange Commission (SEC) on May 5, 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.

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