

Karyopharm Announces Phase 3 BOSTON Study Meets Primary Endpoint with Significant Increase in Progression-Free Survival in Patients with Multiple Myeloma Following One to Three Prior Lines of Therapy

- **Combination of Once-Weekly XPOVIO® (selinexor), Once-Weekly Velcade® (bortezomib) plus Dexamethasone (SVd) Results in Statistically Significant Reduction in the Risk of Disease Progression or Death Compared to Standard Twice-Weekly Velcade® plus Dexamethasone (Vd) Regimen –**
- **47% Increase in Median PFS on SVd versus Vd –**
- **Regulatory Submission Planned in 2Q 2020; Data to be Submitted for Presentation at Upcoming Medical Meetings –**
- **Management to Host Conference Call Today at 8:30 AM ET –**

NEWTON, Mass., March 02, 2020 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), an oncology-focused pharmaceutical company, today announced positive top-line results from the randomized Phase 3 BOSTON study evaluating once-weekly XPOVIO® (selinexor) in combination with once-weekly Velcade® (bortezomib) and low-dose dexamethasone (SVd) compared to standard twice-weekly Velcade plus low-dose dexamethasone (Vd) in patients with multiple myeloma who have received one to three prior lines of therapy. The BOSTON study met its primary endpoint of a statistically significant increase in progression-free survival (PFS). The median PFS in the SVd arm was 13.93 months compared to 9.46 months in the Vd arm, representing a 4.47 month (47%) increase in median PFS (hazard ratio=0.70; p=0.0066). There were no new safety signals on the SVd arm and there was no imbalance in deaths between the two arms in the study. The full top-line data will be submitted for presentation at upcoming medical meetings.

"We are thrilled to report these highly significant top-line results from the BOSTON study, the first randomized Phase 3 trial to demonstrate clinically and statistically significant activity of once-weekly XPOVIO in combination with a current standard of care treatment in patients with myeloma after one to three prior therapies," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "In the study, patients on the SVd regimen lived 47% longer without their disease worsening, which we believe represents an important improvement in the treatment of patients with relapsed or refractory multiple myeloma. We plan to submit the full data set for presentations at upcoming medical meetings to share the results with the medical community. We also intend to submit these data as quickly as possible to the U.S. Food and Drug Administration (FDA) as part of a supplemental New Drug Application seeking to expand the approved indication for XPOVIO into second line treatment for patients with relapsed or refractory multiple myeloma. If approved, the SVd regimen would be the first and only FDA-approved combination drug regimen that includes once-weekly Velcade therapy for relapsed myeloma."

XPOVIO received accelerated approval from the FDA on July 3, 2019 for the treatment of adult patients with relapsed or refractory multiple myeloma 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. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. Karyopharm expects to submit data from the Phase 3 BOSTON study to serve as this confirmatory trial. The full Prescribing Information for XPOVIO is available at www.XPOVIO.com.

About the BOSTON Study

BOSTON is a Phase 3 randomized, active comparator-controlled, open-label, multicenter study that is designed to compare the efficacy, safety and certain health-related quality of life (HR-QoL) parameters of once-weekly XPOVIO (selinexor) in combination with once-weekly Velcade® (bortezomib) plus low-dose dexamethasone (SVd) versus twice-weekly Velcade plus low-dose dexamethasone (Vd) in adult patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy. The BOSTON study enrolled approximately 402 patients. The primary endpoint of the study is progression-free survival (PFS) and key secondary endpoints include overall response rate (ORR), among others. Additionally, the BOSTON study allows for patients on the Vd control arm to crossover to the SVd arm following objective (quantitative) progression of disease. The BOSTON study is being conducted at over 150 clinical sites internationally.

Vd is a standard therapy for previously treated patients with multiple myeloma that is given by injection twice-weekly. Unlike other drugs used to treat multiple myeloma, selinexor is taken orally. Patients randomized to the SVd arm received selinexor (100mg once-weekly), Velcade (1.3 mg/m² once-weekly given subcutaneously) and dexamethasone (40mg weekly). Patients randomized to the Vd arm received Velcade® (twice-weekly) plus low-dose dexamethasone (standard therapy given on the recommended schedule).

Conference Call Information

Karyopharm will host a conference call today, Monday, March 2, 2020, at 8:30 a.m. Eastern Time, to discuss the top-line results from the BOSTON study. To access the conference call, please dial (855) 437-4406 (local) or (484) 756-4292 (international) at least 10 minutes prior to the start time and refer to conference 3515858. 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 Multiple Myeloma

According to the National Cancer Institute (NCI), multiple myeloma is the second most common blood cancer in the U.S. with more than 32,000 new cases each year and over 130,000 patients living with the disease. Despite recent therapeutic advances, there is currently no cure and most patients' disease will typically progress following treatment with currently available therapies. According to the NCI, nearly 13,000 deaths due to multiple myeloma were expected in the U.S. in 2019.

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 recently submitted to 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 from the FDA 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), as a potential backbone therapy in combination with approved 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.

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 Karyopharm Therapeutics

Karyopharm Therapeutics Inc. (Nasdaq: KPTI) is an oncology-focused 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 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 FDA in July 2019 in combination with dexamethasone as a treatment for patients with heavily pretreated multiple myeloma. An MAA for selinexor is also currently under review by the EMA for the same indication. The Company recently submitted a New Drug Application to the FDA seeking approval for XPOVIO in patients with 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 expectations relating to XPOVIO for the treatment of patients with heavily pretreated multiple myeloma or relapsed or refractory diffuse large B-cell lymphoma; 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 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; 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 EU based on the BOSTON study in patients with relapsed or refractory multiple myeloma, or accelerated approval in the U.S. for patients with relapsed or refractory DLBCL as a result of data from the SADAL study, 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: 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 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, 2019, which was filed with the Securities and Exchange Commission (SEC) on February 26, 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.

Velcade® is a registered trademark of Takeda Pharmaceutical Company Limited

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