

## Karyopharm Reports Positive Phase 3 BOSTON Data in Oral Presentation at the American Society of Clinical Oncology 2020 Virtual Scientific Program

*-- Combination of Once-Weekly XPOVIO® (selinexor), Once-Weekly Velcade® (bortezomib) and Dexamethasone (SVd) Prolonged Median Progression-Free Survival by 47% Compared to Standard Twice-Weekly Velcade® plus Dexamethasone (Vd) --*

*-- SVd Was Superior to Vd Across Key Secondary Efficacy Endpoints Including Overall Response Rate, Percent of Patients Achieving ≥VGPR and Median Duration of Response --*

*-- SVd Was Associated with Significantly Lower Rates and Severity of Peripheral Neuropathy Compared to Vd --*

*-- Supplemental New Drug Application Submitted to the FDA Requesting Approval for XPOVIO as a New Treatment for Patients with Multiple Myeloma After At Least One Prior Line of Therapy --*

*-- Conference Call Scheduled for Tomorrow, Friday, May 29, 2020 at 1:00 p.m. ET --*

**NEWTON, Mass.** – May 28, 2020 – Karyopharm Therapeutics Inc. (Nasdaq:KPTI), an innovation-driven pharmaceutical company, today reported detailed results from the pivotal, Phase 3 BOSTON study to be presented at the American Society of Clinical Oncology (ASCO) 2020 Virtual Scientific Program on May 29, 2020. The BOSTON study evaluated once-weekly XPOVIO® (selinexor) in combination with once-weekly Velcade® (bortezomib) and low-dose dexamethasone (40mg weekly) (SVd) compared to standard twice-weekly Velcade plus low-dose dexamethasone (80mg weekly) (Vd) in patients with multiple myeloma who have received one to three prior lines of therapy. As previously reported, the BOSTON study met its primary endpoint with a significant increase in median progression-free survival (PFS) in patients with multiple myeloma following one to three prior lines of therapy.

“In the clinical results to be presented at ASCO this year, once-weekly SVd demonstrated a statistically significant (47%) increase in median PFS compared to the standard twice-weekly Vd regimen and showed a consistent benefit across numerous important patient subgroups such as those who had previously been treated with lenalidomide and those with high-risk cytogenetics,” said Meletios A. Dimopoulos, M.D., Professor and Chairman of the Department of Clinical Therapeutics, National and Kapodistrian University of Athens School of Medicine, and principal investigator of the BOSTON study. “The clinically significant benefits demonstrated in the BOSTON study suggest that, if approved in this expanded patient population, XPOVIO could become an important and more convenient addition in the treatment paradigm for patients after at least one prior line of therapy.”

### Results from the Pivotal Phase 3 BOSTON Study

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[HR]=0.70; p=0.0075). The SVd group also demonstrated a significantly greater overall response rate (ORR) compared to the Vd group (76.4% vs. 62.3%, p=0.0012). Importantly, SVd therapy compared to Vd therapy showed consistent PFS benefit and higher ORR across several important subgroups, including patients 65 years and older, patients who are frail, patients with high-risk

cytogenetics, patients with moderate renal impairment and patients whose disease was refractory to bortezomib or lenalidomide, among others.

In addition, the following results favored SVd therapy as compared to Vd therapy:

- SVd therapy demonstrated a significantly higher rate of deep responses, defined as  $\geq$  Very Good Partial Response (VGPR) compared to Vd therapy (44.6% vs. 32.4%) as well as a longer median duration of response (20.3 months vs. 12.9 months). Additionally, 16.9% of patients on the SVd arm achieved a Complete Response (CR) or a Stringent Complete Response (sCR) as compared to 10.6% of patients receiving Vd therapy. All responses were confirmed by an Independent Review Committee (IRC).
- Data at the time of analysis showed a trend toward an overall survival (OS) benefit associated with SVd therapy with fewer deaths, numerically, reported on the SVd arm (47 vs. 62). Median OS for the SVd arm had not yet been reached as of the data cut-off date of February 18, 2020 while the median OS for the Vd arm was 25.0 months. The median OS for the SVd arm will be reported once it is reached and becomes available.
- Peripheral neuropathy rates were significantly lower on SVd compared to Vd (32.3% vs. 47.1%;  $p=0.0010$ ).

The most common treatment-related adverse events (AEs) were cytopenias, along with gastrointestinal and constitutional symptoms and were consistent with those previously reported from other selinexor studies. Most AEs were manageable with dose modifications and/or standard supportive care. The most common non-hematologic treatment-related AEs were nausea (50%), fatigue (42%), decreased appetite (35%), and diarrhea (32%) and were mostly Grade 1 and 2 events. The most common Grade 3 and 4 treatment-related AEs were thrombocytopenia (40%), anemia (16%), and fatigue (13%). Peripheral neuropathy was the most common AE that led to treatment discontinuation on both arms, however, the rate of peripheral neuropathy was significantly lower in the SVd group compared to the Vd group (32% vs. 47%;  $p=0.0010$ ). The average duration of therapy on SVd was 10 months, and the discontinuation rate due to AEs was 17% on the SVd arm compared to 11% on the Vd arm.

The once-weekly SVd regimen utilizes 40% less Velcade and 25% less dexamethasone and requires  $\sim$ 37% fewer clinic visits during the first 24 weeks of treatment compared to the standard Vd regimen. Because Velcade is given as a subcutaneous injection rather than as an infusion, clinic visits may be shorter with the SVd regimen than with other non-Velcade regimens that may be employed to treat relapsed multiple myeloma and require intravenous infusions.

A supplemental New Drug Application (sNDA) has been submitted to the U.S. Food and Drug Administration (FDA) requesting approval for XPOVIO in combination with Velcade and low dose dexamethasone as a new treatment for patients with previously treated multiple myeloma. The Company also plans to submit a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) requesting approval for the same indication later this year.

“We are honored to share the full, positive results from the pivotal Phase 3 BOSTON study with the oncology community at ASCO 2020, and we believe the successful outcome of this study represents an important advancement for myeloma patients, their families and physicians,” said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. “We would like to express our sincere gratitude to all of the patients and investigators who participated in the BOSTON study. The sNDA requesting approval for XPOVIO as a new, second line treatment for patients with multiple myeloma has now been submitted to the FDA and we look

forward to working closely with regulatory authorities to make this potential new treatment option available to the oncology community as quickly as possible.”

### About the BOSTON Study

BOSTON was a Phase 3 randomized, active comparator-controlled, open-label, multicenter study 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 402 patients. The primary endpoint of the study was progression-free survival (PFS) and key secondary endpoints included overall response rate (ORR), rate of peripheral neuropathy, and others. Additionally, the BOSTON study allowed for patients on the Vd control arm to crossover to the SVd arm following objective (quantitative) progression of disease verified by an IRC. The BOSTON study was 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/m<sup>2</sup> 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).

### Details for the ASCO 2020 Virtual Scientific Program presentation is as follows:

#### *Late-breaking Oral Presentation*

**Title:** Weekly Selinexor, Bortezomib, and Dexamethasone (SVd) Versus Twice Weekly Bortezomib and Dexamethasone (Vd) in Patients with Multiple Myeloma (MM) After 1-3 Prior Therapies: Initial Results of the Phase 3 BOSTON

**Presenter:** Meletios A. Dimopoulos, *National and Kapodistrian University of Athens School of Medicine*

**Abstract #:** 8501

**Session:** Hematologic Malignancies—Plasma Cell Dyscrasia

**Date and time:** 05/29/2020, 8:00 AM – 11:00 AM

**URL:** <https://meetinglibrary.asco.org/record/186143/abstract>

### Conference Call Information

Karyopharm will host a conference call tomorrow, Friday, May 29, 2020, at 1:00 p.m. Eastern Time, to discuss the detailed Phase 3 BOSTON study results. The call will feature recognized myeloma expert Paul Richardson, MD, Clinical Program Leader and Director of Clinical Research at the Jerome Lipper Multiple Myeloma Center, Dana-Farber Cancer Institute, and R.J. Corman Professor of Medicine at Harvard Medical School, along with members of the Karyopharm executive leadership team. To access the conference call, please dial (484) 756-4292 (local) or (855) 437-4406 (international) at least 10 minutes prior to the start time and refer to conference ID [2049236]. 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 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](http://www.clinicaltrials.gov).

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

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Email: [medicalinformation@karyopharm.com](mailto:medicalinformation@karyopharm.com)

### **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-HT<sub>3</sub> 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  $\geq 3$  infections were reported in 25% of patients, and deaths resulting from an infection occurred in 4% of patients. The most commonly reported Grade  $\geq 3$  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](http://www.XPOVIO.com).

### 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](http://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 XPOVIO's ability to treat patients with multiple myeloma and expectations related to other XPOVIO 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.

Velcade® is a registered trademark of Takeda Pharmaceutical Company Limited.

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