Karyopharm Presents XPOVIO® (Selinexor) Data in Multiple Myeloma and Diffuse Large-B-Cell Lymphoma at the American Society of Hematology 2020 Annual Meeting

-- Pomalyst®, Kyprolis® and Revlimid® Arms of the Phase 1b/2 STOMP Study Evaluating Once Weekly XPOVIO with Low-Dose Dexamethasone Combinations Continue to Demonstrate Favorable Response Rates and Durability in Patients with Previously Treated Multiple Myeloma --
-- Multiple Subgroup Analyses from the Phase 3 BOSTON Study Demonstrate that XPOVIO Is Effective and Well Tolerated Regardless of Prior Lines of Treatment and Across Several Important Patient Subgroups, Including Patients with High Risk Cytogenetics and the Elderly and Frail --
-- Multiple Subgroup Analyses from the Phase 2b SADAL Study Show that XPOVIO is Effective and Well Tolerated Across Important Patient Subgroups, Including Those with Renal Dysfunction and the Elderly --
-- 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 that over twenty presentations related to XPOVIO® (selinexor), the Company's first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound, were presented at the American Society of Hematology (ASH) 2020 Annual Meeting taking place virtually December 5-8, 2020. These presentations included:

- An oral presentation highlighted updated data from the Pomalyst® (pomalidomide) arm of the Phase1b/2 **STOMP** study evaluating XPOVIO in combination with backbone therapies in patients with relapsed or refractory multiple myeloma;
- Updated data from the Kyprolis®(carfilzomib) and Revlimid® (lenalidomide) arms of the STOMP study;
- Several new subgroup analyses from the pivotal Phase 3**BOSTON** study evaluating once weekly XPOVIO in combination with once weekly Velcade® (bortezomib) and low-dose dexamethasone (SVd) versus standard twice weekly Velcade® with dexamethasone (Vd) in adult patients with multiple myeloma following one to three prior lines of therapy;
- New subgroup analyses from the Phase 2b **SADAL** study evaluating XPOVIO in relapsed or refractory diffuse large B-cell lymphoma (DLBCL).

"The highlights of our ASH data this year include updated data from multiple arms of the STOMP study where once weekly oral XPOVIO continues to demonstrate compelling and durable responses in important patient subgroups when combined with approved multiple myeloma therapies. We believe that XPOVIO has the potential to be an important combination partner for future multiple myeloma treatment regimens," said Sharon Shacham, PhD, MBA, Founder, President and Chief Scientific Officer of Karyopharm. "Several presentations were also given describing subgroup analyses from the Phase 3 BOSTON study. Collectively, these analyses show that XPOVIO is effective and well tolerated regardless of prior lines of treatment, including prior treatment with a proteasome inhibitor or lenalidomide, and across several important patient subgroups including those with high risk cytogenetics and the elderly and the frail. Notably, the highest progression free survival (PFS) seen across these subgroups came from patients who were naïve to proteasome inhibitor therapy whose median PFS had not yet been reached, as well as from those who had previously been treated with only one prior therapy who demonstrated a median PFS of 16.6 months in the SVd arm compared to 10.6 months in the Vd arm. A supplemental New Drug Application seeking approval for XPOVIO for the patient population studied in the BOSTON study is currently being reviewed by the U.S. Food and Drug Administration and has been assigned a target Prescription Drug User Fee Act action date of March 19, 2021. If approved, we expect to launch in the expanded indication immediately thereafter."

Updated Data from Phase 1b/2 STOMP Study Evaluating the All Oral Regimen of XPOVIO in Combination with Pomalyst® and Low-dose Dexamethasone (SPd) in Patients with Relapsed or Refractory Multiple Myeloma

In this all oral arm of the Phase1b/2 STOMP study, XPOVIO is being evaluated in combination with Pomalyst®and low-dose dexamethasone in patients with relapsed or refractory multiple myeloma who received at least two prior lines of therapy, including a proteasome inhibitor (PI) and an immunomodulatory drug (IMiD). Of note, 25% of the population enrolled in the study had previously received Darzalex®. The recommended Phase 2 dose (RP2D) was determined to be XPOVIO 60mg orally once-weekly, Pomalyst® 4mg orally once-daily and dexamethasone orally (40mg once weekly or 20mg twice weekly). The following table is a summary of the efficacy results:

	Best Responses[1] in Evaluable SPd Patients as of November 14, 2020[2]					
Category	**N**	**ORR**	**CR**	**VGPR**	**PR**	**Median PFS**

Pomalyst® naïve or non-refractory	46	25 (54%)	1 (2%)	9 (20%)[3]	15 (33%)[4]	12.3 months
Pomalyst® refractory	14	5 (36%)	-	1 (7%)	4 (29%)	Not reported
RP2D	20	12 (60%)	-	6 (30%)	6 (30%)	Not reached[5]
All patients	60	30 (50%)	1 (2%)	10 (17%)	19 (32%)	12.2 months

Key: ORR=Overall Response Rate (CR+VGPR+PR); CR=Complete Response; VGPR=Very Good Partial Response; PR=Partial Response

[1] Responses were adjudicated according to the International Myeloma Working Group (IMWG) criteria

[2] Based on interim unaudited data

[3] Two VGPRs were unconfirmed

[4] One PR was unconfirmed

[5] Median follow-up time for 20 patients at the RP2D was 2.5 months; median follow-up time for all 60 patients was 12.2 months

Among the patients evaluated for safety as of the data cutoff date, the most common treatment-related adverse events (AEs) were cytopenias, along with gastrointestinal and constitutional symptoms; most were manageable with dose modifications and/or standard supportive care. The most common non-hematologic treatment-related AEs were nausea (60%), fatigue (51%), decreased appetite (44%), weight loss (38%) and diarrhea (29%), and were primarily grade 1 and 2 events. As expected, the most common treatment-related Grade 3 and 4 AEs were neutropenia (54%), anemia (33%), and thrombocytopenia (32%).

Based on these Phase 2 results, a Phase 3 study investigating the SPd combination (XPORT-MM-031) is planned to begin in 2021. Historical clinical trials evaluating the efficacy of Pomalyst® and low-dose dexamethasone in less heavily pretreated populations (i.e., without prior Darzalex® therapy) have demonstrated an overall response rate of 29% and median PFS of 3.6 months, as highlighted in the Pomalyst® U.S. Full Prescribing Information.

Updated Data from Phase 1b/2 STOMP Study Evaluating XPOVIO in Combination with Kyprolis® and Low-dose Dexamethasone (SKd) in Patients with Relapsed or Refractory Multiple Myeloma

In this arm of the Phase 1b/2 STOMP study, oral XPOVIO is being evaluated in combination with Kyprolis® and low-dose dexamethasone in patients with relapsed or refractory multiple myeloma who have received at least two prior therapies, including a PI, one or more IMiDs (e.g., Revlimid® or Pomalyst®) or Darzalex®. In these heavily pretreated patients, 100% had previously received Velcade®, 96% had previously received Revlimid®, 67% had previously received Pomalyst® and 63% had previously received Darzalex®. The RP2D was determined to be XPOVIO 80mg orally once-weekly, Kyprolis® 56mg/m^2 once-weekly and dexamethasone (40mg orally once weekly or 20mg twice weekly) and enrollment continues using this regimen. The following table is a summary of the efficacy results:

Best Responses[1] in Evaluable SKd Patients as of October 1, 2020[2]					
Category	**N**	**ORR**	**CR**	**VGPR**	**PR**
All	24	18 (75%)	5 (21%)	8 (33%)	5 (21%)

[1] Responses were adjudicated according to the IMWG criteria

[2] Based on interim unaudited data

Median PFS was 23.7 months for all patients.

Among the patients evaluated for safety as of the data cutoff date, the most common treatment-related AEs were cytopenias, along with gastrointestinal, constitutional and other symptoms; most were manageable with dose modifications and/or standard supportive care. The most common non-hematologic treatment-related AEs were nausea (71%), fatigue (58%), decreased appetite (50%) and weight loss (46%), and were mostly Grade 1 and 2 events. As expected, the most common treatment-related Grade ≥3 AEs included thrombocytopenia (58%), anemia (21%) and leukopenia (13%).

These results indicate that the once weekly combination of SKd can induce responses in the majority of patients with heavily pretreated double or triple class refractory myeloma.

Updated Data from Phase 1b/2 STOMP Study Evaluating the All Oral Regimen of XPOVIO in Combination with Revlimid® and Low-dose Dexamethasone (SRd) in Patients with Newly Diagnosed and Relapsed or Refractory (RR) Multiple Myeloma

In this all oral arm of the Phase 1b/2 STOMP study, XPOVIO is being evaluated in combination with Revlimid® and low-dose dexamethasone in patients with newly diagnosed or previously treated multiple myeloma. The previously treated patients

received at least one prior therapy, which may include prior Revlimid®, as long as the patient's myeloma was not refractory to Revlimid®. The RP2D was determined to be XPOVIO (60mg orally, once-weekly), Revlimid® (25mg orally, once daily), and dexamethasone (40mg orally, once weekly or 20mg twice weekly). The following table is a summary of the efficacy results:

Best Responses[1] in Evaluable SRd Patients as of October 1, 2020[2]					
Category	**N**	**ORR**	**CR**	**VGPR**	**PR**
Revlimid®-naïve RR myeloma	12	11 (92%)	1 (8%)	4 (33%)	6 (50%)[3]
Revlimid®-treated/refractory myeloma	8	1 (13%)	-	-	1 (13%)
Newly diagnosed (efficacy evaluable)	7[4]	7 (100%)	1 (14%)	4 (57%)[5]	2 (29%)

[1] Responses were adjudicated according to the IMWG criteria

[2] Based on interim unaudited data

[3] Two PRs were unconfirmed

[4] One patient's efficacy not evaluable due to withdrawal of consent during cycle 1

[5] One VGPR was unconfirmed

Responses are highly durable with four relapsed or refractory patients remaining on study with PFS of greater than 35 months and two newly diagnosed patients remaining on study with PFS of greater than 24 months.

Among the newly diagnosed patients evaluable for safety, the most common treatment-related AEs were cytopenias, along with gastrointestinal and constitutional symptoms; most were manageable with dose modifications and/or standard supportive care. The most common non-hematologic treatment-related AEs were fatigue (63%), weight loss (63%), diarrhea (63%), nausea (50%) and insomnia (38%) and were mostly Grade 1 and 2 events. The most common Grade ≥3 AEs were neutropenia (75%), anemia (50%) and thrombocytopenia (38%).

Among the relapsed or refractory patients evaluable for safety, the most common treatment-related AEs were cytopenias, along with gastrointestinal and constitutional symptoms; most were manageable with dose modifications and/or standard supportive care. The most common non-hematologic treatment-related AEs were nausea (58%), fatigue (54%), decreased appetite (50%), weight loss (42%), and diarrhea (33%), and were mostly Grade 1 and 2 events. The most common Grade ≥3 AEs were thrombocytopenia (63%), neutropenia (63%), anemia (17%) and fatigue (17%).

These data show that the all oral regimen of weekly selinexor with standard Revlimid® and dexamethasone induces high response rates with good tolerability.

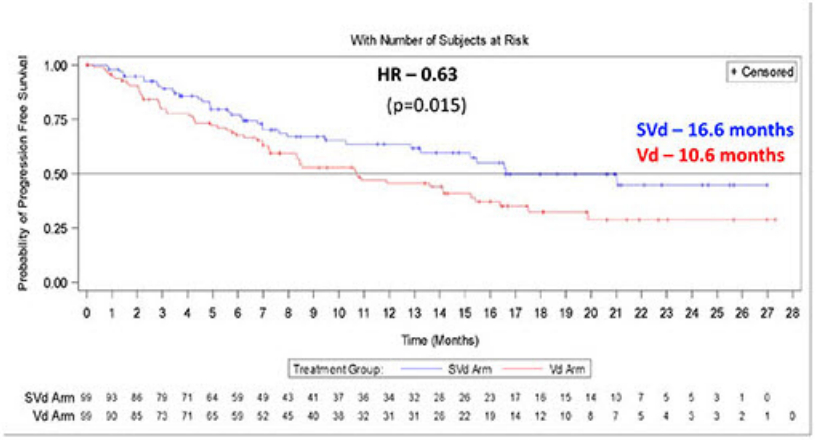
Phase 3 BOSTON Study Subgroup Analyses in Multiple Myeloma Following One to Three Prior Lines of Therapy

The pivotal Phase 3 BOSTON study evaluated once weekly XPOVIO in combination with once weekly Velcade® and low-dose dexamethasone (SVd) versus standard twice weekly Velcade® and moderate dose dexamethasone (Vd) in adult patients with multiple myeloma following one to three prior lines of therapy. Karyopharm previously reported positive data from this study which were recently published in the Lancet. The subgroup analyses presented at ASH 2020 include evaluations of the safety and efficacy of XPOVIO (i) in patients previously treated with PIs, (ii) according to the number of prior lines of therapy or prior treatment with Revlimid®, (iii) in patients with high risk cytogenetics, and (iv) based on age (patients younger than 65 years old versus older than 65 years old) or by frailty level (frail versus fit).

- **Patients previously treated with PIs.** Among the 402 patients treated in the BOSTON study, 307 (76%) had prior treatment with a PI (e.g., Velcade®) and 95 (24%) were PI naïve. Among patients who were PI-naïve, median PFS was not yet reached for patients receiving SVd versus 9.7 months for patients on the Vd arm (HR 0.26; p=0.0003). In patients previously treated with a PI, SVd improved PFS relative to Vd with an HR of 0.78 (p=0.057). Among patients who only had a Velcade® based induction regimen prior to autologous stem cell transplant (ASCT), SVd provided a PFS benefit compared to Vd with an HR of 0.58 (p=0.06). ORR was significantly improved with SVd in PI-treated patients (77% versus 60%; p=0.0006). The ≥VGPR rate was 41.9% in patients on SVd versus 29.6% on Vd (p=0.012) and 53.2% on SVd versus 41.7% on Vd (p=0.131) in the prior PI and PI naïve groups, respectively. Non-peripheral neuropathy (PN) AEs were higher with SVd, however, most of these AEs were reversible and treatable; PN AEs were consistently higher in all subgroups on Vd as compared with SVd. These results suggest that SVd is an active, convenient regimen and may have a particularly strong benefit in patients with previously treated myeloma who have not yet received a PI or had a Velcade®-based ASCT induction regimen. Importantly, although the doses of Velcade® and dexamethasone were substantially lower on the SVd arm as compared with the Vd arm, SVd still conferred benefits over Vd in patients who had previously received Velcade®.
- **Prior lines of therapy and prior treatment with Revlimid®.** Among the 402 patients treated in the BOSTON study, 154 (38%) had previously received Revlimid® and 204 (51%) had received at least two prior lines of therapy. This analysis demonstrated that SVd was active regardless of prior Revlimid® treatment with a PFS HR of 0.63 (p=0.017) among patients with prior Revlimid® treatment who received SVd compared to patients treated with Vd. Notably, patients who had only received one prior therapy prior to enrolling in the BOSTON study achieved a PFS of 16.6 months on SVd

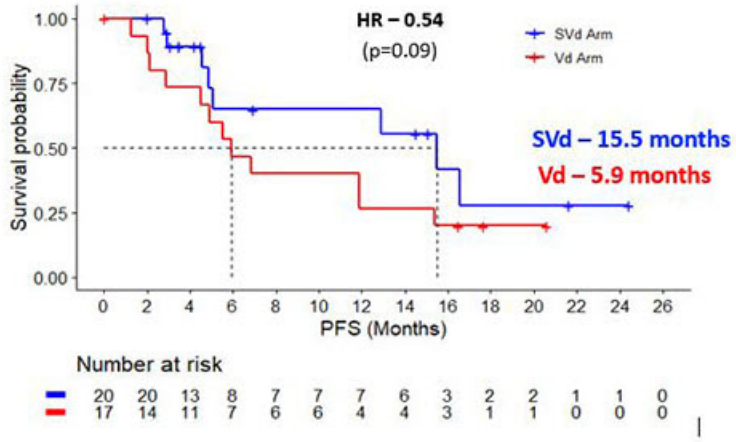
compared to 10.6 months for Vd (HR 0.63; p=0.015) (see Figure 1). Also, regardless of prior treatment, SVd was associated with significantly lower rates of Grade 2 or higher PN compared to Vd. AEs of Grade ≥3 were more commonly reported in the SVd treatment arm than in the Vd arm, however, most non-PN AEs were reversable and treatable and major organ toxicities were not common. These results suggest that, if approved, SVd may offer an effective and convenient treatment option for patients with previously treated multiple myeloma, including those that have been treated with Revlimid®. SVd may confer its strongest benefits to patients who have received a single line of therapy including Revlimid®, though it was numerically superior in all of the subgroups evaluated.

Figure 1. Patients with One Prior Regimen (PFS Graph)



- **Patients with high risk cytogenetics.** Among the 402 patients treated in the BOSTON study, 141 (35%) had high risk cytogenetics, defined as patients with at least one abnormality (i.e., chr(17p) deletion, t(4;14), t(14;16), or amplification with ≥4 copies of chr(1q21)) in ≥10% of screened plasma cells. This analysis demonstrated that SVd was superior to Vd in patients with high risk multiple myeloma, including in patients with one cytogenetic abnormality, two or more abnormalities and in patients with a chr(17p) deletion (i.e., patients with myeloma missing one copy of the p53 tumor suppressor protein). In patients with one cytogenetic abnormality, patients treated with SVd achieved a PFS of 10.2 months compared to 8.6 months for Vd treated patients (HR 0.69; p=0.08) while patients with ≥2 cytogenetic abnormalities treated with SVd achieved a PFS of 15.5 months compared to 5.9 months for Vd treated patients (HR 0.54; p=0.09) (see Figure 2). The safety profile of SVd and Vd in both higher risk and standard risk groups were consistent with the overall BOSTON population. Non-PN AEs were higher with SVd and most of the AEs were reversible. These results suggest that SVd is an effective and safe regimen and, if approved, may be an important treatment option for patients with high risk multiple myeloma.

Figure 2. Patients with ≥2 Cytogenetic Abnormalities (PFS Graph)



- **Patients stratified by age (<65 or ≥65) and frailty.** Among the 402 patients treated in the BOSTON study, 241 (60%) were at least age 65 and 130 (32%) were characterized as frail. This analysis demonstrated that both elderly and frail patients benefited from SVd compared to Vd. Elderly patients treated with SVd achieved a PFS of 21.0 months compared to 9.4 months for Vd treated patients (HR 0.55; p=0.002). SVd also provided a statistically significant PFS benefit in frail

patients: 13.9 months for SVd treated patients compared to 9.4 months for Vd treated patients, (HR 0.69; p=0.08). Overall, SVd prolonged PFS, improved response rates and had lower rates of PN regardless of age and frailty score compared to Vd. Non-PN AEs were higher with SVd and most of the AEs were reversible and treatable. These results suggest that SVd, if approved, may be an effective and well tolerated treatment option for patients with previously treated multiple myeloma, including those who are elderly or frail.

Phase 2b SADAL Study in Patients with relapsed or refractory DLBCL Subgroup Analyses

The Phase 2b SADAL study evaluated twice weekly XPOVIO in adult patients with relapsed or refractory DLBCL, not otherwise specified, who had received at least two prior therapies. Karyopharm previously reported positive data from this study and the data were published in The Lancet Haematology. The subgroup analyses presented at ASH 2020 included evaluations of the safety and efficacy of XPOVIO in patients stratified by (i) age and (ii) renal function at baseline. An additional poster was also presented highlighting the results of a study in which researchers investigated molecular markers of response to XPOVIO in patients treated on the SADAL study.

- **Patients stratified by age (<65 or ≥65).** Among the 134 patients treated in the SADAL study, 82 (61%) were at least age 65. This analysis demonstrated that patients ≥65 years old had similar clinical benefit to those <65 years old when treated with XPOVIO. There was no statistical difference in ORR in patients <65 years old versus ≥65 years old. Median duration of response was also similar at 9.7 months in the <65 years old patient group compared to 9.2 months in the ≥65 years old patient group. The incidence of treatment-related AEs was comparable between both groups. The most common Grade ≥3 AEs in <65 vs ≥65 years old patients were thrombocytopenia (42.3% vs 39.0%), nausea (3.8% vs 7.3%), and fatigue (5.8% vs 13.4%). These results suggest that XPOVIO is an active, convenient oral option for patients with relapsed or refractory DLBCL, including the elderly.
- **Patients stratified by renal function at baseline.** Among the 134 patients treated in the SADAL study, 37 (28%) had low creatinine clearance (CrCl) defined as CrCl of ≤60mL/min. This analysis demonstrated that XPOVIO had similar response rates in patients regardless of severity of renal function. Treatment with XPOVIO demonstrated a similar ORR in patients with a baseline reduced CrCl (29.7%) compared to normal CrCl (28.9%). Overall survival was also comparable in patients with reduced versus normal renal function: 7.8 vs 9.1 months. The incidence of treatment-related AEs was comparable between both groups. The most common Grade ≥3 treatment-related AEs for patients with reduced versus normal renal function were thrombocytopenia (45.9% vs. 38.1%), nausea (5.4% vs. 6.2%), and fatigue (8.1% vs. 11.3%).These results suggest that XPOVIO is an important option for patients with relapsed or refractory DLBCL, including patients with renal dysfunction.

PDF copies of all of these presentations are available **here**.

Virtual Investor and Analyst Event Conference Call and Webcast

Karyopharm will host a conference call and webcast tomorrow, Tuesday, December 8, 2020, from 1:00 to 2:30 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 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 relapsed or refractory 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 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; 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.

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https://investors.karyopharm.com/2020-12-07-Karyopharm-Presents-XPOVIO-R-Selinexor-Data-in-Multiple-Myeloma-and-Diffuse-Large-B-Cell-Lymphoma-at-the-American-Society-of-Hematology-2020-Annual-Meeting