Karyopharm Announces New Selinexor Data in Myelofibrosis and Multiple Myeloma to be Presented at ASH 2022

– Encouraging Data Observed in Phase 1 Study of Selinexor in Combination with Ruxolitinib in Treatment-Naïve Myelofibrosis, Including Activity Across Three Key Efficacy Endpoints of Spleen Volume Reduction, Symptom Improvement, and Hemoglobin Stabilization, with a Generally Manageable Tolerability Profile and No Dose Limiting Toxicities–

– New Data on Triple Class Refractory Multiple Myeloma Patients Continue to Highlight the Efficacy and Tolerability of Selinexor in the Treatment of Multiple Myeloma –

NEWTON, Mass., Nov. 3, 2022 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced that two abstracts detailing new selinexor data have been selected for poster presentation at the 64th American Society of Hematology (ASH) Annual Meeting and Exposition taking place December 10-13, 2022. The presentations include results from the Phase 1 open-label, dose-escalation study of selinexor in combination with ruxolitinib in patients with treatment-naïve myelofibrosis (MF) and data from a subset analysis of the STOMP study in patients with triple-class refractory MM.

Results from Phase 1 Study Evaluating Selinexor in Combination with Ruxolitinib in Patients with Treatment-Naïve Myelofibrosis

The data included in the abstract for ASH 2022 were based on the Phase 1 portion of the Phase 1/2 study evaluating the safety and preliminary efficacy of once-weekly selinexor in combination with standard dose ruxolitinib in patients with treatment-naïve myelofibrosis (NCT04562389). As of July 2022, 19 patients had been assigned to either selinexor 40 mg or 60 mg, in combination with ruxolitinib 15/20 mg BID.

Seventy-nine percent of efficacy evaluable patients (11 out of 14) demonstrated ≥35% reduction in spleen volume (SVR35) at week 12 and 86% (6 out of 7) achieved SVR35 at week 24. Thirteen patients who had received at least 12 weeks of treatment experienced rapid improvements in their symptom scores, with 69% (9 out of 13) of efficacy evaluable patients having ≥50% reduction (TSS50). Eleven out of 17 transfusion-independent patients (65%) who had at least eight weeks of treatment maintained stable hemoglobin (± 2g/dL) or improved hemoglobin level (>2g/dL increase) at last follow up.

"We remain very encouraged by the notable activity across three clinically meaningful efficacy endpoints relevant to patients with MF including spleen volume reduction, improvement in symptom score and hemoglobin stabilization," said Reshma Rangwala, MD, PhD, Chief Medical Officer of Karyopharm. "We look forward to observing how the efficacy and safety evolve across the two doses and engaging with the FDA on the registrational portion of this trial."

The data observed across both the 40mg and 60mg assigned groups demonstrate a generally manageable side effect profile with no dose-limiting toxicities observed at either dose level in the Phase 1a dose escalation portion of the study. The most common adverse events (AEs) were nausea (58%), anemia (42%) and vomiting (42%), the majority of which were grades 1-2. The most common reported grade 3-4 treatment-emergent AEs were thrombocytopenia (26%) and anemia (21%), both of which were reversible. Updated data from this study, including results from additional patients, will be presented at the ASH meeting in December 2022.

"The addition of novel agents to JAK inhibitors is an intriguing approach to improve depth and duration of responses compared to JAK inhibition alone," said Dr. Haris Ali, City of Hope Comprehensive Cancer Center. "The introduction of a novel mechanism of SINE inhibition, in combination with a JAK inhibitor, may provide patients an upfront treatment option that could improve clinical outcomes with a manageable safety profile."

Details for the ASH 2022 abstracts are as follows:

Poster Presentations

Title: A Phase 1, Open-Label, Dose-Escalation Study of Selinexor Plus Ruxolitinib in Patients with Treatment-Naïve Myelofibrosis
Presenter: Dr. Ali, City of Hope Comprehensive Cancer Center
Abstract #: 1734
Session Type: Poster Presentation
Session: 634. Myeloproliferative Syndromes: Clinical and Epidemiological: Poster I
Date and Time: Saturday, December 10, 2022, 5:30 PM - 7:30 PM CT

Title: Once Weekly Selinexor, Carfilzomib and Dexamethasone (XKd) in Triple Class Refractory Multiple Myeloma

Presenter: Dr. Schiller, David Geffen School of Medicine at UCLA
Abstract #: 4516
Session Type: Poster Presentation
Session: 652. Multiple Myeloma and Plasma Cell Dyscrasias: Clinical and Epidemiological: Poster III
Date and Time: Monday, December 12, 2022, 6:00 PM - 8:00 PM CT

Online Publication

Title: Real-World Safety and Effectiveness of Selinexor-Based Regimens in Patients with Relapsed or Refractory Multiple Myeloma and Dialysis-Dependent Renal Impairment
Presenter: Dr. Niblock, Karyopharm Therapeutics
Abstract #: 5773
Session Type: Online publication
Date and Time: Available in the November supplemental issue of Blood

About XPOVIO® (selinexor)

XPOVIO is a first-in-class, oral exportin 1 (XPO1) inhibitor and the first of Karyopharm's Selective Inhibitor of Nuclear Export (SINE) compounds to be approved for the treatment of cancer. XPOVIO functions by selectively binding to and inhibiting the nuclear export protein XPO1. XPOVIO is approved in the U.S. and marketed by Karyopharm in multiple oncology indications, including: (i) in combination with Velcade® (bortezomib) and dexamethasone (XVd) in patients with multiple myeloma after at least one prior therapy; (ii) in combination with dexamethasone in patients with heavily pre-treated multiple myeloma; and (iii) in patients with diffuse large B-cell lymphoma (DLBCL), including DLBCL arising from follicular lymphoma, after at least two lines of systemic therapy. XPOVIO (also known as NEXPOVIO® in certain countries) has received regulatory approvals in various indications in a growing number of ex-U.S. territories and countries, including but not limited to the European Union, the United Kingdom, China, South Korea, Canada, Israel and Taiwan. XPOVIO and NEXPOVIO is marketed by Karyopharm's partners, Antengene, Menarini, Neopharm and FORUS in China, South Korea, Singapore, Australia, Hong Kong, Germany, Austria, Israel and Canada.

Please refer to the local Prescribing Information for full details.

Selinexor is also being investigated in several other mid- and late-stage clinical trials across multiple high unmet need cancer indications, including in endometrial cancer and myelofibrosis.

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

SELECT IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- Thrombocytopenia: Monitor platelet counts throughout treatment. Manage with dose interruption and/or reduction and supportive care.
- Neutropenia: Monitor neutrophil counts throughout treatment. Manage with dose interruption and/or reduction and granulocyte colony–stimulating factors.
- Gastrointestinal Toxicity: Nausea, vomiting, diarrhea, anorexia, and weight loss may occur. Provide antiemetic prophylaxis. Manage with dose interruption and/or reduction, antiemetics, and supportive care.
- Hyponatremia: Monitor serum sodium levels throughout treatment. Correct for concurrent hyperglycemia and high serum paraprotein levels. Manage with dose interruption, reduction, or discontinuation, and supportive care.
- Serious Infection: Monitor for infection and treat promptly.
- Neurological Toxicity: Advise patients to refrain from driving and engaging in hazardous occupations or activities until neurological toxicity resolves. Optimize hydration status and concomitant medications to avoid dizziness or mental status changes.
- Embryo–Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential and males with a female partner of reproductive potential, of the potential risk to a fetus and use of effective contraception.
- Cataract: Cataracts may develop or progress. Treatment of cataracts usually requires surgical removal of the cataract.

Adverse Reactions

- The most common adverse reactions (≥20%) in patients with multiple myeloma who receive XVd are fatigue, nausea, decreased appetite, diarrhea, peripheral neuropathy, upper respiratory tract infection, decreased weight, cataract and vomiting. Grade 3–4 laboratory abnormalities (≥10%) are thrombocytopenia, lymphopenia, hypophosphatemia, anemia, hyponatremia and neutropenia. In the BOSTON trial, fatal adverse reactions occurred in 6% of patients within 30 days of last treatment. Serious adverse reactions occurred in 52% of patients. Treatment discontinuation rate due to adverse

reactions was 19%.

- The most common adverse reactions (≥20%) in patients with multiple myeloma who receive Xd are thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea and upper respiratory tract infection. In the STORM trial, fatal adverse reactions occurred in 9% of patients. Serious adverse reactions occurred in 58% of patients. Treatment discontinuation rate due to adverse reactions was 27%.
- The most common adverse reactions (incidence ≥20%) in patients with DLBCL, excluding laboratory abnormalities, are fatigue, nausea, diarrhea, appetite decrease, weight decrease, constipation, vomiting, and pyrexia. Grade 3–4 laboratory abnormalities (≥15%) are thrombocytopenia, lymphopenia, neutropenia, anemia, and hyponatremia. In the SADAL trial, fatal adverse reactions occurred in 3.7% of patients within 30 days, and 5% of patients within 60 days of last treatment; the most frequent fatal adverse reactions was infection (4.5% of patients). Serious adverse reactions occurred in 46% of patients; the most frequent serious adverse reaction was infection (21% of patients). Discontinuation due to adverse reactions occurred in 17% of patients.

Use In Specific Populations

Lactation: Advise not to breastfeed.

For additional product information, including full prescribing information, please visit**www.XPOVIO.com.**

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. Since its founding, Karyopharm has been an industry leader in oral Selective Inhibitor of Nuclear Export (SINE) compound technology, which was developed to address a fundamental mechanism of oncogenesis: nuclear export dysregulation. Karyopharm's lead SINE compound and first-in-class, oral exportin 1 (XPO1) inhibitor, XPOVIO® (selinexor), is approved in the U.S. and marketed by the Company in three oncology indications and has received regulatory approvals in various indications in a growing number of ex-U.S. territories and countries, including Europe and the United Kingdom (as NEXPOVIO®) and China. Karyopharm has a focused pipeline targeting multiple high unmet need cancer indications, including in multiple myeloma, endometrial cancer, myelodysplastic syndromes and myelofibrosis. For more information about our people, science and pipeline, please visit www.karyopharm.com, and follow us on Twitter at@Karyopharm and LinkedIn.

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 the ability of selinexor to treat patients with multiple myeloma, myelofibrosis, diffuse large B-cell lymphoma, solid tumors and other diseases; and expectations related to the clinical development plans and potential regulatory submissions of 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 or that any of Karyopharm's drug candidates, including selinexor and eltanexor, 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 obtain and 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 enroll patients in its clinical trials; unplanned cash requirements and expenditures; development or regulatory approval of drug candidates by Karyopharm's competitors for products or product candidates in which Karyopharm is currently commercializing or developing; and Karyopharm's ability to obtain, maintain and enforce patent and other intellectual property protection for any of its products or product candidates. These and other risks are described under the caption "Risk Factors" in Karyopharm's Quarterly Report on Form 10-Q for the quarter ended June 30, 2022, which

was filed with the Securities and Exchange Commission (SEC) on August 4, 2022, 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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