

Karyopharm Announces Presentation of Updated Phase 1 Selinexor Data in Patients with Treatment-Naïve Myelofibrosis at ASH 2022

- A 92% SVR35 and a 67% TSS50 were Observed in the Efficacy Evaluable Patients at Week 24 -
- 57% of Transfusion Independent Patients Achieved Hemoglobin Stabilization -
- Company to Host Investor and Analyst Webcast Featuring Key Opinion Leaders Today at 8:30 a.m. ET -

NEWTON, Mass., Dec. 12, 2022 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced updated results from the Phase 1 portion of its study evaluating the safety and efficacy of once-weekly selinexor in combination with standard dose ruxolitinib in patients with treatment-naïve myelofibrosis (NCT04562389). The data, featured in a poster presentation at the 64th American Society of Hematology (ASH) 2022 Annual Meeting and Exposition, show that the combination of selinexor with ruxolitinib achieved rapid and sustained spleen responses, encouraging improvements in symptoms and stabilization of hemoglobin levels in patients with treatment-naïve myelofibrosis.

As of October 21, 2022, 24 patients had been assigned to either a 40 mg or 60 mg once weekly dose of selinexor, in combination with ruxolitinib 15/20 mg BID (twice daily). At week 24, 92% of efficacy evaluable patients (11 out of 12) demonstrated $\geq 35\%$ reduction in spleen volume (SVR35). Ongoing reductions in SVR were seen from baseline to week 12 and week 24, with a 45% median reduction at week 12 and a 49% median reduction at week 24. 67% of the evaluable patients for symptom response (4 out of 6) at week 24 achieved $\geq 50\%$ reduction (TSS50). 57% of transfusion-independent patients (13 out of 23) maintained or improved their hemoglobin levels.

"As an oral agent with a unique mechanism of action, selinexor has previously shown single-agent activity in myelofibrosis patients," said Reshma Rangwala, MD, PhD, Chief Medical Officer of Karyopharm. "As a result, we believe that the combination of selinexor and ruxolitinib has the potential to meaningfully build upon the current standard of care, which is ruxolitinib alone, for patients with treatment-naïve myelofibrosis. We look forward to further developing this combination in the randomized phase of the study."

The safety population was comprised of 24 patients, all of whom received at least one dose of selinexor. The most common adverse events (AEs) were nausea (75%), anemia (62%) and fatigue (58%), the majority of which were grades 1-2. The most common reported grade 3-4 treatment-emergent AEs were anemia (37%) and thrombocytopenia (21%), both of which were reversible.

"In the Phase 1 portion of the study, encouraging efficacy was observed across the relevant efficacy endpoints of SVR35, TSS50, and hemoglobin stabilization and a generally manageable safety profile was observed regardless of dose. Furthermore, I find the rapid spleen reduction as early as week 12 especially notable, along with early signs of durability," said Dr. Haris Ali, City of Hope Comprehensive Cancer Center. "These data support the potential of an oral XPO1 inhibitor, in combination with a JAK inhibitor, to deliver significant benefits for patients with myelofibrosis."

Investor and Analyst Event on Selinexor Data in Patients with Treatment-Naïve Myelofibrosis at ASH 2022

Karyopharm will host a webcast today, December 12, 2022, at 8:30 a.m. Eastern Time (7:30 a.m. CT local time), featuring key opinion leaders Dr. Haris Ali, City of Hope Comprehensive Cancer Center and Dr. Srdan Verstovsek, MD Anderson Cancer Center. Drs. Ali and Verstovsek will discuss the updated data on selinexor in combination with ruxolitinib as well as the current treatment landscape and unmet medical need in treating patients with myelofibrosis, respectively.

To access the event, the live audio webcast and slides 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 following the event.

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 ($\geq 20\%$) 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 ($\geq 10\%$) 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 ($\geq 20\%$) 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 $\geq 20\%$) in patients with DLBCL, excluding laboratory abnormalities, are fatigue, nausea, diarrhea, appetite decrease, weight decrease, constipation, vomiting, and pyrexia. Grade 3-4 laboratory abnormalities ($\geq 15\%$) 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](https://twitter.com/Karyopharm) and [LinkedIn](https://www.linkedin.com/company/karyopharm).

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 September 30, 2022, which was filed with the Securities and Exchange Commission (SEC) on November 3, 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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