Karyopharm Shares Data at ASH 2023 Showing Strong SVR and TSS Durability Observed from Phase 1 Study of Selinexor 60mg and Ruxolitinib in JAK Inhibitor (JAKi)-Naïve Myelofibrosis Patients, with no SVR or TSS Progressions Observed As of the Data Cutoff(1)

Biomarker Data from Phase 1 Study of Selinexor in Combination with Ruxolitinib in Treatment-Naïve Myelofibrosis (MF) Suggestive of Disease Modification

Data Reinforce the Potential for Selinexor in Combination with Ruxolitinib to Become a Novel, First-Line Treatment for JAKi-Naïve Patients with MF

NEWTON, Mass., Dec. 10, 2023 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced long-term follow up of treatment-naïve patients with myelofibrosis (MF) who participated in the Phase 1 portion of its study evaluating once-weekly selinexor in combination with ruxolitinib (NCT04562389). The data, featured in an oral presentation at the 65th American Society of Hematology Annual Meeting and Exposition (ASH 2023), show patients treated with 60mg selinexor, and who achieved ≥35% reduction in spleen volume (SVR35) at week 24, continued to remain in radiographic response. In addition, all patients who achieved TSS50 at Week 24 remained in response as of the data cut-off.

The data included in the oral presentation for ASH 2023 were based on the Phase 1 portion of the Phase 1/3 study evaluating the safety and efficacy of once-weekly selinexor in combination with ruxolitinib in patients with treatment-naïve MF (NCT04562389). As of August 1, 2023, 24 patients had been assigned to either selinexor 40mg (N= 10) or 60mg (N=14), in combination with ruxolitinib. The maximum duration of follow-up was 78 weeks with a median duration of 32 weeks for SVR35 durability, and a maximum duration of follow-up was 64 weeks with a median duration of 51 weeks for TSS50 durability.

An exploratory biomarker analysis showed a reduction of variant allele frequency (VAF) at week 24 for all three MF driver genes (*CALR, MPL, and JAK2*) and rapid and sustained reduction of pro-inflammatory cytokine production. Early cytokine reduction at Week 4 was associated with spleen volume reduction (SVR) at Week 24 and was sustained until the end of treatment. The clinical efficacy associated with biomarkers impacting MF biological hallmarks may suggest disease modification.

"The growing body of data from this study suggests that selinexor in combination with ruxolitinib may provide spleen reduction, symptom improvement, long-term durability and disease modification, expanding the benefit this combination may provide to patients with treatment-naïve myelofibrosis, " said Reshma Rangwala, MD, PhD, Chief Medical Officer of Karyopharm. "We're excited about the potential to change treatment paradigms for these patients – and expand the number of patients who benefit from first-line therapy."

The safety profile was consistent with previous data cuts with no new safety signals observed as of Aug 1st.

"The current standard of care is not associated with consistent molecular or pathologic responses," said DrSri Tantravahi, University of Utah. "The long-term findings are very exciting as they underscore the potential for durable, clinically relevant responses and modification of disease course. The wait for new options has been long and difficult for the myelofibrosis community, and we welcome this important research to help advance the understanding of XPO1 and JAK inhibitor combinations as a meaningful treatment option for patients."

"We are encouraged by the attention MPNs (Myeloproliferative Neoplasms) are getting in recent years from companies like Karyopharm," said Kapila Viges, Chief Executive Officer of MPN Research Foundation. "With patients waiting for more answers to these chronic yet serious blood cancers, we look forward to the data readouts at ASH this year. Efforts to develop better therapies and now combinations of therapies bring hope to the myelofibrosis community and open the potential for more options in the treatment paradigm. For patients, options matter."

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 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; the direct or indirect impact of the COVID-19 pandemic or any future pandemic on Karyopharm's business, results of operations and financial condition; 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, 2023, which was filed with the Securities and Exchange Commission (SEC) onNovember 2, 2023, 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.

References:

[1] For SVR 35: Events defined as less than or equal to 35% spleen volume reduction from baseline and more than 25% increase in spleen volume from Nadir, assessed radiographically. For TSS50: Events defined as a total symptom score that is equal to or exceeds the baseline value. As of August 1, 2023 data cut off.

SOURCE Karyopharm Therapeutics Inc.

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