Karyopharm Announces Presentation of Updated Phase 1 Selinexor Data in Patients with Treatment-Naïve Myelofibrosis at AACR 2023

– At Week 24, 60mg of Selinexor in Combination with Ruxolitinib Achieved: 92% SVR35 and 78% TSS50 in Efficacy Evaluable Population, 79% SVR35 and 58% TSS50 in Intent to Treat Population –

– Rapid, Deep, Sustained Spleen Response Across all Subgroups, Robust Symptom Improvement with a Generally Tolerable and Manageable Side Effect Profile; 60mg Selinexor is the Recommended Dose in Combination with Ruxolitinib –

– Planning to Initiate Pivotal Phase 3 Study in Front-Line Myelofibrosis in 1H 2023 –

– Company to Host Investor Webcast with Key Opinion Leader Dr. John Mascarenhas, Professor of Medicine at the Icahn School of Medicine at Mount Sinai, Today at 4:30 p.m. ET –

NEWTON, Mass., April 18, 2023 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced updated results from the Phase 1 study evaluating the safety and efficacy of once-weekly selinexor in combination with ruxolitinib in patients with treatment-naïve myelofibrosis (NCT04562389). The data, featured in a poster presentation at the American Association for Cancer Research (AACR) Annual Meeting 2023, show that rapid, deep and sustained spleen responses and robust symptom improvement were achieved at both weeks 12 and 24, in patients treated with selinexor 60mg in combination with ruxolitinib.

As of the February 24, 2023 data cut-off date, 24 patients had been assigned to either a 40mg or 60mg once weekly dose of selinexor, combined with ruxolitinib. All patients initiated treatment > 24 weeks prior to the data cut-off date.

Key Findings

Efficacy
SVR35 (≥35% reduction in spleen volume) and TSS50 (≥50% reduction in total symptom score)

- **60mg of selinexor**
  - Week 12
    - Efficacy evaluable population: 83.3% SVR35 and 80.0% TSS50
    - Intent to treat population: 71.4% SVR35 and 66.7% TSS50
  - Week 24
    - Efficacy evaluable population: 91.7% SVR35 and 77.8% TSS50
    - Intent to treat population: 78.6% SVR35 and 58.3% TSS50
  - SVR35 responses were observed in 100% of evaluable patients at any time and rates were consistent regardless of subgroups, including males and patients treated with low dose ruxolitinib.
  - Improvement in major spleen and cytokine-related symptoms were observed across all MFSAF (Myelofibrosis Symptom Assessment Form) domains.
- **40mg of selinexor**
  - Week 12
    - Efficacy evaluable population: 30.0% SVR35 and 66.7% TSS50
    - Intent to treat population: 30.0% SVR35 and 60.0% TSS50
  - Week 24
    - Efficacy evaluable population: 50.0% SVR35 and 57.1% TSS50
    - Intent to treat population: 40.0% SVR35 and 40.0% TSS50

Safety

- Both the 40mg and 60mg dose levels of selinexor were generally well tolerated and manageable, allowing most patients to remain on therapy, up to 68 weeks, as of the data cut-off date.
- The most common treatment emergent adverse events (TEAEs), regardless of grade, experienced with the 40mg and 60mg selinexor doses, respectively, in combination with ruxolitinib were nausea (70.0%; 78.6%), anemia (40.0%; 64.3%) and fatigue (60.0%; 57.1%), most of which were grades 1-2.
- The most common treatment emergent grade ≥3 adverse events experienced with the 40mg and 60mg selinexor doses, respectively, in combination with ruxolitinib were anemia (30.0%; 42.9%), thrombocytopenia (10.0%, 28.6%) and neutropenia (20.0%; 7.1%).
- There were two treatment-related discontinuations, one due to thrombocytopenia and one due to peripheral neuropathy.
- 75% of nausea events were grade 1, were mostly transient and did not lead to treatment-related discontinuations. Nausea rates and grades were reduced for patients who received prophylactic antiemetics. Meaningful weight gain was observed at week 24 despite the incidence of nausea.

"We are enthusiastic about the impressive spleen volume reductions and robust symptom improvement observed with the 60mg dose of selinexor and ruxolitinib combination at week 24, which represent very meaningful improvements relative to the current standard of care of ruxolitinib alone. These data suggest that the combination of selinexor and ruxolitinib has the potential to be a transformative therapy for first line myelofibrosis patients," said Reshma Rangwala, MD, PhD, Chief Medical Officer of Karyopharm. "We are also very encouraged by the preliminary data showing rapid normalization in platelets and stability of hemoglobin levels, as potential evidence of disease modification for these patients. We look forward to building upon these findings as we plan the initiation of a pivotal Phase 3 study in front-line myelofibrosis later this quarter."

"There remains significant unmet need in the treatment of myelofibrosis, with less than half of patients achieving an SVR35 with the current standard of care therapy," said Dr. Haris Ali, City of Hope Comprehensive Cancer Center. "The spleen responses and symptom improvements seen across all patients with the 60mg selinexor dose is very compelling. These data suggest this tolerable and unique combination of XPO1 and JAK inhibition has the potential to significantly improve these key efficacy measures for first line myelofibrosis patients."

Both the efficacy and safety data support the 60 mg dose of selinexor as the recommended dose in combination with ruxolitinib. A double-blind, randomized, Phase 3 trial of selinexor 60 mg in combination with ruxolitinib versus placebo in combination with ruxolitinib in JAKi treatment-naïve patients with myelofibrosis is expected to initiate in the first half of 2023.

Investor Webcast on Selinexor Data in Patients with Treatment-Naïve Myelofibrosis at AACR 2023
Karyopharm will host a webcast today, April 18, 2023, at 4:30 p.m. Eastern Time, with key opinion leader Dr. John Mascarenhas, Professor of Medicine at the Icahn School of Medicine at Mount Sinai and Director of the Center of Excellence for Blood Cancers and Myeloid Disorders. Dr. Mascarenhas will discuss the relevance of the updated data with selinexor in combination with ruxolitinib to the current treatment landscape and unmet medical need in treating patients with myelofibrosis. He will also describe the design of the Company's selinexor and ruxolitinib Phase 3 study as the study's primary investigator.

To access the event, please dial (888) 349-0102 (local) or (412) 902-4299 (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, along with accompanying 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 (≥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 neoplasms 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 myelofibrosis; and expectations related to the clinical development of selinexor 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 Annual Report on Form 10-K for the year ended December 31, 2022, which was filed with the Securities and Exchange Commission (SEC) on February 17, 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.

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