Karyopharm's Phase 3 SENTRY Trial in Myelofibrosis Met First Co-Primary Endpoint, Demonstrating Statistically Significant Improvement in Spleen Volume Reduction

– While Similar Symptom Improvement Was Observed Across the Two Arms Relative to Baseline, SENTRY Did Not Meet its Second Co-Primary Endpoint of Abs-TSS –

– SENTRY Demonstrated a Rapid and Near Doubling of Patients Achieving SVR35 at Week 24, versus Ruxolitinib –

– Promising Overall Survival Signal with >50% Reduction of Risk of Death versus Ruxolitinib –

– Evidence of Potential Disease Modification with More Patients Achieving ≥20% Reductions in VAF as Early as Week 24 versus Ruxolitinib –

– No New Safety Signals Identified –

– Karyopharm will Meet with the FDA to Discuss the Totality of the Data and Potential sNDA Filing –

– Conference Call Scheduled for Today at 8:00 a.m. ET –

NEWTON, Mass., March 24, 2026 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today reported topline results from its Phase 3 SENTRY trial, a randomized, double-blind, placebo-controlled trial of 60 mg selinexor in combination with ruxolitinib in frontline myelofibrosis (n=353). The trial met the first co-primary endpoint, demonstrating statistically significant improvement in spleen volume reduction of 35% or more (SVR35) for patients treated with the combination of selinexor plus ruxolitinib, with rapid, deep and sustained spleen volume reduction rates seen in the combination arm. The mean change in absolute total symptom score (Abs-TSS) at week 24 relative to baseline was comparable across the two arms with similar symptom improvement relative to baseline; the difference across the two arms was not statistically significant. Importantly, the topline results suggest a promising signal in overall survival (OS) for the combination arm.

- **Spleen Volume:** 50% of patients who received the combination of selinexor plus ruxolitinib achieved a statistically significant improvement in SVR35 at week 24 compared to 28% of patients who received ruxolitinib alone (one-sided $p<0.0001$). Patients on the combination achieved rapid spleen reduction with 49% already achieving SVR35 at week 12 compared to 20% who received ruxolitinib alone. Spleen volume reduction was sustained, with 47% of patients on the combination achieving SVR35 at week 36 compared to 23% who received ruxolitinib alone.

- **Symptoms:** Similar symptom improvement from baseline was observed in patients who received the combination of selinexor plus ruxolitinib compared to ruxolitinib alone as measured by Abs-TSS at week 24. Patients who received the combination reported a 9.89 point improvement in Abs-TSS compared to a 10.86 point improvement in patients who received ruxolitinib alone.

- **Overall Survival:** Promising OS signal was observed in patients who received the combination of selinexor plus ruxolitinib compared to ruxolitinib alone with a hazard ratio of 0.43 (95% CI [0.19, 1.00] nominal one-sided $p=0.0222$). The Company intends to continue to follow OS to maturity to further evaluate this signal.

- **Overall Survival Associated with SVR35:** Post-hoc landmark analyses at weeks 12 and 24 suggest SVR35 may predict overall survival.

- **Variant Allele Frequency (VAF) Reduction:** Evidence of potential disease modification from a pre-specified exploratory endpoint was observed at week 24 from baseline in the combination arm as 32% of patients who received the combination achieved a ≥20% reduction in VAF for JAK2, MPL, and CALR compared to 24% of patients who received ruxolitinib alone (n=261).

- **Other Secondary and Exploratory Endpoints:** Across other secondary and exploratory endpoints of progression-free survival, hemoglobin stabilization, and bone marrow fibrosis improvement, no meaningful difference was observed between the trial arms as of the data cut-off of February 20, 2026. The Company intends to further evaluate these endpoints as they mature.

Patients were randomized 2:1 to 60 mg of selinexor once weekly plus ruxolitinib or placebo plus ruxolitinib. The ruxolitinib dose was determined based on the patients' baseline platelet count per the drug's prescribing information. All data presented are as of the data cut-off of February 20, 2026.

"The results from SENTRY are an important development for patients as the combination of selinexor plus ruxolitinib meaningfully improved spleen response and we observed a promising signal in overall survival. Reducing spleen volume remains one of the most important treatment goals in myelofibrosis since achieving SVR35 is associated with improvement in overall survival," said 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. "While the symptom endpoint did not reach statistical significance, patients treated in both arms achieved similar symptom improvement relative to baseline. Importantly, while JAK inhibitors have been the backbone of therapy, continued progress requires new therapies that target additional biological pathways. Inhibition of XPO1 represents a differentiated mechanism that has the potential to address these pathways and evolve treatment beyond JAK inhibition alone."

"For patients with myelofibrosis, improvements in spleen and symptoms are expected outcomes from JAK inhibitors such as ruxolitinib. The SENTRY topline results suggest that the combination of selinexor and ruxolitinib delivers superior spleen reduction, which may predict overall survival, while offering similar symptom improvement, and may offer an important advance for our patients," said Dr. Claire Harrison, Professor of Myeloproliferative Neoplasms and Deputy Chief Medical Officer of Research, Data, and Analytics at Guy's and St. Thomas' NHS Foundation Trust in the United Kingdom.

"Selinexor's differentiated mechanism provides a complementary approach to JAK inhibition and highlights the importance of targeting additional biological pathways beyond JAK signaling to further advance outcomes for patients with myelofibrosis. I am encouraged by the speed and magnitude of spleen response, and the promising overall survival signal and evidence of potential disease modification. In totality, these data underscore selinexor's potential to meaningfully improve clinical outcomes for patients with myelofibrosis," said Reshma Rangwala, MD, PhD, Chief Medical Officer and Head of Research of Karyopharm. "On behalf of Karyopharm, I would like to thank the patients, families, caregivers, investigators, and clinical trial team who participated in this trial. We are excited to share our results with regulatory authorities, key opinion leaders and patient advocacy organizations."

"The myelofibrosis community is waiting for new treatment options that can build upon the benefit of JAK inhibitors. Improving overall survival is the ultimate goal for people living with myelofibrosis and I am incredibly encouraged by these results," said Kapila Viges, Chief Executive Officer of the MPN Research Foundation. "These results are an exciting development for the myelofibrosis community."

Safety and Tolerability

The combination demonstrated a manageable safety and tolerability profile consistent with the known profile of selinexor and ruxolitinib individually. No new safety signals were observed.

The five most common all-grade treatment emergent adverse events (TEAEs) in the selinexor plus ruxolitinib arm were thrombocytopenia (selinexor plus ruxolitinib arm: 59%; placebo plus ruxolitinib arm: 43%), anemia (57%; 58%), nausea (57%; 17%), constipation (32%; 36%) and neutropenia (27%; 9%) (n=234; n=116). The rate of grade 3+ TEAEs was 70% in the selinexor plus ruxolitinib arm compared to 50% in the placebo plus ruxolitinib arm. The rate of TEAEs leading to treatment discontinuation was 15% in the selinexor plus ruxolitinib arm and 9% in the placebo plus ruxolitinib arm. The rate of confirmed leukemic transformations was the same across both arms of the trial at 1.7%.

Next Steps

The Company will be meeting with the U.S. Food and Drug Administration (FDA) to discuss the totality of the data from the SENTRY trial and its supplemental new drug application (sNDA) filing plan.

The Company plans to share additional data from the Phase 3 SENTRY trial at an upcoming medical meeting and expects to submit a manuscript to a peer-reviewed medical journal. The Company believes that potential inclusion in relevant compendia could occur in the second half of 2026.

Conference Call Information

Karyopharm will host a conference call today, March 24, 2026, at 8:00 a.m. Eastern Time, to discuss the results of its Phase 3 SENTRY trial in myelofibrosis. To access the conference call, please dial (800) 836-8184 (local) or (646) 357-8785 (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. An archived webcast will be available on the Company's website approximately two hours after the event.

About the Phase 3 SENTRY Trial

SENTRY (XPORT-MF-034; NCT04562389) is a Phase 3 clinical trial evaluating a once-weekly dose of 60 mg of selinexor in combination with ruxolitinib compared to placebo plus ruxolitinib in JAKi-naïve myelofibrosis patients with platelet counts ≥100 x 10^9/L. Patients were randomized 2-to-1 to the selinexor arm. The co-primary endpoints for this trial are spleen volume reduction ≥ 35% (SVR35) at week 24 and the average change in absolute total symptom score (Abs-TSS) over 24 weeks relative to baseline.

About Myelofibrosis

Myelofibrosis is a rare blood cancer that affects approximately 20,000 patients inthe United States and 17,000 patients in the European Union[1]. The disease causes bone marrow fibrosis (scarring in the bone marrow), which makes it difficult for the bone marrow to make healthy blood cells, splenomegaly (enlarged spleen), progressive anemia which often leads to symptoms like fatigue and weakness, and other disease associated symptoms including abdominal discomfort, pain under the left ribs, early satiety, night sweats and bone pain. The only approved class of therapies to treat myelofibrosis are JAK inhibitors, including ruxolitinib.

1. Clarivate/DRG (2023)

About XPOVIO® (selinexor)

XPOVIO is a first-in-class, oral exportin 1 (XPO1) inhibitor compound 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 adult patients with multiple myeloma after at least one prior therapy; (ii) in combination with dexamethasone in adult patients with heavily pre-treated multiple myeloma; and (iii) under accelerated approval in adult 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, Mainland China, Taiwan, Hong Kong, Australia, South Korea, Singapore, Israel, and Canada. XPOVIO®/NEXPOVIO® is marketed in these respective ex-U.S. territories by Karyopharm's partners: Antengene, Menarini, Neopharm, and FORUS. Selinexor is also being investigated in several other mid- and late-stage clinical trials across multiple high unmet need cancer indications, including in myelofibrosis and endometrial cancer.

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

XPOVIO® (selinexor) is a prescription medicine approved:

- In combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy (XVd).
- In combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma 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 (Xd).
- For the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least two lines of systemic therapy. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

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 whose dedication to pioneering novel cancer therapies is fueled by a belief in the extraordinary strength and courage of patients with cancer. Since its founding, Karyopharm has been an industry leader in oral compounds that address nuclear export dysregulation, a fundamental mechanism of oncogenesis. Karyopharm's lead 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. It has also received regulatory approvals in various indications in 50 ex-U.S. territories and countries, including the European Union, the United Kingdom (as NEXPOVIO®) and China. Karyopharm has a focused pipeline targeting indications in multiple high unmet need cancers, including in multiple myeloma, endometrial cancer, myelofibrosis, and diffuse large B-cell lymphoma (DLBCL). For more information about our people, science and pipeline, please visit www.karyopharm.com, and follow us on LinkedIn and on X at @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, endometrial cancer, myelofibrosis, diffuse large B-cell lymphoma and other diseases; expectations with respect to the clinical development plans, regulatory discussions and potential regulatory submissions for selinexor; and expectations regarding the timing, presentation and publication of additional data from the Phase 3 SENTRY trial. 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, 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 trials, including subsequent analysis of existing data and new data received from ongoing and future trials; 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 trials; 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; substantial doubt exists regarding Karyopharm's ability to continue as a going concern; 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, 2025, which was filed with the Securities and Exchange Commission (SEC) on February 13, 2026, 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.

SOURCE Karyopharm Therapeutics Inc.

For further information: Investors: Brendan Strong, Senior Vice President, Investor Relations, 617.762.2661, brendan.strong@karyopharm.com; Media: Mary Ann Ondish, Head of Corporate Communications, 914.552.4625, Maryann.ondish@karyopharm.com

---

https://investors.karyopharm.com/2026-03-24-Karyopharms-Phase-3-SENTRY-Trial-in-Myelofibrosis-Met-First-Co-Primary-Endpoint,-Demonstrating-Statistically-Significant-Improvement-in-Spleen-Volume-Reduction