

Karyopharm Announces Preliminary Unaudited 2023 Revenue and 2024 Objectives

- Accelerating Innovation and Growth Strategy with Top-Line Data Readouts Expected in 2H 2024 and 2025 from Three Pivotal Phase 3 Studies Evaluating Selinexor in Multiple Myeloma, Endometrial Cancer and Myelofibrosis -

- Preliminary Unaudited Full Year 2023 Total Revenue and U.S. XPOVIO® (selinexor) Net Product Revenue Expected to be Approximately \$146 Million and \$112 Million, Respectively, Meeting Company's Guidance -

- Potential for Selinexor to be a Novel Maintenance Treatment for Patients with TP53 Wild-Type Endometrial Cancer Further Strengthened with Long-Term Exploratory Subgroup Analyses from SIENDO Study; Recruitment Ongoing in the Company's Pivotal Phase 3 Study; Further Updates Planned to be Presented in 2024 -

- Opportunity to Define a New Myelofibrosis Treatment Paradigm Based on the Encouraging Data Presented from the Phase 1 Study of Selinexor in Combination with Ruxolitinib in Patients with Treatment-Naïve Myelofibrosis; Recruitment Ongoing in the Company's Pivotal Phase 3 Study; Further Updates Planned to be Presented in 2024 -

- Expect Cash Runway into Late 2025 Supporting Company Through Multiple Potentially Value Generating Milestones -

NEWTON, Mass., Jan. 8, 2024 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced preliminary unaudited fourth quarter and full year 2023 total revenue and U.S. XPOVIO net product revenue estimates and outlined its 2023 achievements and 2024 objectives.

"2023 was a year focused on accelerating our prioritized late-stage pipeline with updated data readouts from our studies in endometrial cancer and myelofibrosis, strengthening our potential to significantly improve outcomes for patients. We focused our resources and delivered on our revenue guidance as we continued to expand use of selinexor amidst a highly competitive multiple myeloma landscape. In 2024, we will continue to concentrate our investments to rapidly advance our pipeline and strengthen our foundation in multiple myeloma and deliver value for patients and our shareholders with multiple value driving catalysts expected throughout 2024," said Richard Paulson, President and Chief Executive Officer of Karyopharm.

Key Program Highlights in 2023

Selinexor in Multiple Myeloma (MM)

- Total demand for XPOVIO grew in the community setting, which accounted for approximately two-thirds of XPOVIO net product revenue; in the academic setting, demand for XPOVIO was adversely impacted by increased competitive pressures in the later lines.
- XPOVIO net product revenue was adversely impacted year-over-year by increased utilization of the KaryForward Patient Assistance Program (PAP), due to multiple myeloma foundation closures¹, contributing to ~10% of total demand in 2023 as compared to ~5% in 2022, leading to ~\$6 million impact. Additionally, increased competition and higher gross-to-net, driven by increased 340B discounts and Medicaid rebates during the year, adversely impacted XPOVIO net product revenue.
- XPOVIO continued its strategic shift to earlier lines, with patient mix approaching 70% in the second to fourth lines versus 55% in 2022², contributing to an increase in duration of therapy.
- The National Comprehensive Cancer Network® (NCCN) Clinical Practice Guidelines elevated XPOVIO in combination with bortezomib (Velcade®) and dexamethasone (XVd) to a preferred and category 1 regimen for lenalidomide-refractory patients with relapsed or refractory multiple myeloma who have received one-to-three prior lines of therapy [in the September 2023 Clinical Practice Guidelines in Oncology](#).
- Clinical trial collaboration agreement executed with Bristol Myers Squibb (BMS) to evaluate selinexor in combination with BMS' proprietary investigational cereblon E3 ligase modulator (CELMoD™) agent mezigdomide in patients with relapsed/refractory multiple myeloma progressing after T-cell

immunotherapies, adding to the growing combinations with selinexor that have shown benefit in multiple myeloma and enabling further evaluation of selinexor's role in maintaining an optimal T-cell environment.

- Selinexor has been approved in more than 40 countries and recently achieved national reimbursement in mainland China. In 1Q 2023, the Company's license agreement with the Menarini Group was expanded to include the Middle East and Africa regions.

Selinexor in Endometrial Cancer (EC)

- Long-term exploratory subgroup analysis of the pre-specified subgroup of patients with advanced or recurrent *TP53* wild-type EC from the Phase 3 SIENDO study (NCT03555422) was presented at medical conferences, with updated progression free survival and preliminary data showing improvement in overall survival.
- The SIENDO study manuscript was published in the Journal of Clinical Oncology.

Selinexor in Myelofibrosis (MF)

- Presented updated results from the Phase 1 study (XPORT-MF-034) evaluating selinexor in combination with ruxolitinib in patients with treatment-naïve MF at several medical conferences demonstrating encouraging spleen reduction, symptom improvement, long-term durability and disease modification data.
- Initiated pivotal Phase 3 portion of the XPORT-MF-034 clinical trial (NCT04562389) to assess the efficacy and safety of once-weekly selinexor 60mg in combination with ruxolitinib in JAKi-naïve patients with MF.
- Received Fast Track Designation from the U.S. Food and Drug Administration (FDA) for selinexor for the treatment of patients with MF, including primary MF, post-essential thrombocythemia MF, and post-polycythemia vera MF.
- Planned Phase 2 XPORT-MF-044 study (NCT05980806) to evaluate the efficacy and safety of selinexor monotherapy in subjects with JAK inhibitor-naïve MF and moderate thrombocytopenia. Entered into an agreement with SOBI for the supply of pacritinib as an optional add-on in the study for eligible patients.

Eltanexor in Myelodysplastic Neoplasms (MDS)

- Reported interim data from the Phase 2 study of single-agent eltanexor in high risk relapsed/refractory MDS (NCT02649790).
- Further development of eltanexor in MDS is on hold in line with the Company's prioritization of its late-stage pipeline programs.

Intellectual Property

- The United States Patent and Trademark Office issued a certificate extending the term of the patent covering the composition of matter of XPOVIO[®] (selinexor) (U.S. patent 8,999,996) by 342 days to July 3, 2033.
- The U.S. Patent and Trademark Office has issued patents directed toward the polymorphic form of selinexor present in XPOVIO, pharmaceutical compositions comprising the polymorphic form and methods of treatment using the polymorphic form and the pharmaceutical compositions. The newly issued patents will expire in August 2035.

Optimization of Corporate Organization

- Further positioned the Company's organization to focus on and invest in its Phase 3 programs and drive agile execution of business priorities, through optimization of its cost structure with a ~ 20% reduction of the workforce, including full-time employees and contractors.

Corporate and Financial Highlights for 2023

- Based on preliminary unaudited financial information, the Company expects total revenue, which includes license and royalty revenue from partners, to be approximately \$33.6 million for the fourth quarter 2023 and approximately \$145.9 million for the full year 2023, and U.S. XPOVIO net product revenue to be approximately \$25.0 million for the fourth quarter 2023 and approximately \$112.0 million for the full year 2023, meeting Company's guidance.

- Cash, cash equivalents, restricted cash and investments as of December 31, 2023 was approximately \$192.0 million, enabling an expected cash runway into late 2025.

The financial information presented in this press release may be adjusted as a result of the completion of customary annual review and audit procedures.

Near-Term Catalysts and Operational Objectives Anticipated in 2024

- Report top-line results from pivotal Phase 3 study evaluating an oral combination of selinexor, pomalidomide and dexamethasone in patients with previously treated MM in 2H 2024.
- Publish and present efficacy and safety data on selinexor 40mg in combination with pomalidomide and dexamethasone from ongoing STOMP/028 Phase 2 studies in patients with MM.
- Report additional data on selinexor's preservation of T-cell fitness and potential combinability with multiple agents pre or post T-cell therapy in patients with MM.
- Complete enrollment in pivotal EC-042 Phase 3 trial in TP53 wild-type EC.
- Present updated exploratory subgroup analysis results in patients with TP53 wild-type EC from the SIENDO study.
- Report updated results from the Phase 1 study of selinexor in combination with ruxolitinib in patients with treatment-naïve MF.
- Report preliminary results from Phase 2 study evaluating the efficacy and safety of selinexor monotherapy in subjects with JAK inhibitor-naïve MF and moderate thrombocytopenia.
- Maintain the Company's commercial foundation in the competitive MM marketplace, driving increased XPOVIO revenues.
- Continue global launches and reimbursement approvals for selinexor by partners in ex-U.S. territories.

Listen to the Webcast

These achievements and updates will be discussed during a webcast presentation at the 42nd Annual J.P. Morgan Healthcare Conference to be held on January 10, 2024, at 5:15 p.m. Eastern Time/2:15 p.m. Pacific Time. A live webcast of the presentation and breakout session, along with accompanying slides, can be accessed under "Events & Presentations" in the Investor section of the Company's website, <http://investors.karyopharm.com/events-presentations>. An archived replay will be available for 30 days following the event. The presentation slides will also 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 a growing number of ex-U.S. territories and countries, including Europe, the United Kingdom, China, South Korea and Israel, and is marketed in those areas by Karyopharm's global partners. 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

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 ($\geq 20\%$) 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 neoplasms and myelofibrosis. For more information about our people, science and pipeline, please visit <https://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 Karyopharm's preliminary financial information for the fourth quarter and full year 2023; guidance on its expected cash runway; expectations with respect to commercialization efforts; the ability of selinexor or eltanexor to treat patients with multiple myeloma, endometrial cancer, myelofibrosis, diffuse large B-cell lymphoma, myelodysplastic neoplasms and other diseases; and expectations with respect to the clinical development plans and potential regulatory submissions of selinexor and eltanexor. 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) on November 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.

XPOVIO® and NEXPOVIO® are registered trademarks of Karyopharm Therapeutics Inc. Any other trademarks referred to in this release are the property of their respective owners.

References:

¹ Four multiple myeloma foundations provide financial support to Medicare patients with multiple myeloma

² Based on Komodo claims data analysis, accessed in October 2023

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