Karyopharm Reports Fourth Quarter and Full Year 2023 Financial Results and Highlights Recent Company Progress

– Total Revenue of $146 Million and U.S. XPOVIO® (selinexor) Net Product Revenue of $112 Million for Full Year 2023, Meeting Company's Guidance –

– Top-Line Data Readouts from Three Pivotal Phase 3 Trials Evaluating Selinexor in Endometrial Cancer, Myelofibrosis and Multiple Myeloma Expected in 2025 –

– Company Provides Full-Year 2024 Total Revenue Guidance of $140 Million to $160 Million, Including U.S. XPOVIO Net Product Revenue Guidance of $100 Million to $120 Million; Cash Runway to Late 2025 –

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

NEWTON, Mass., Feb. 29, 2024 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today reported financial results for the fourth quarter and full year ended December 31, 2023. In addition, Karyopharm highlighted select corporate milestones and provided an overview of its key clinical development programs.

"We made significant progress in 2023 across our clinical pipeline and continued to build on our foundation in the highly competitive multiple myeloma space. The encouraging clinical results that we presented last year reinforce the potential of our three ongoing pivotal Phase 3 trials in addressing critical unmet needs of cancer patients," said Richard Paulson, President and Chief Executive Officer of Karyopharm. "Our drive for innovation and progress will continue into 2024, by focusing our resources to advance our Phase 3 trials. We are enthusiastic about the upcoming top-line read-outs from these trials and what they could mean for patients and selinexor's growth potential."

Fourth Quarter 2023 and Recent Highlights

Research and Development (R&D) Highlights

- Long-term exploratory analysis of the pre-specified subgroup of patients with advanced or recurrent *TP53* wild-type endometrial cancer (EC) from the Phase 3 SIENDO trial (NCT03555422) was presented at the International Gynecological Cancer Society Annual Global Meeting in Seoul, South Korea, with updated progression-free survival (PFS). As of the September 1, 2023 data cut-off date, median PFS was 27.4 months in the selinexor treatment arm (n=77) as compared to 5.2 months (n=36) in the placebo arm. Immature overall survival data showed an encouraging signal and corroborated the PFS results.

- Oral presentation at the 65th American Society of Hematology 2023 Annual Meeting of the updated results from the Phase 1 trial (XPORT-MF-034) evaluating selinexor in combination with ruxolitinib in patients with treatment-naïve myelofibrosis (MF) showed encouraging long-term durability. 79% of intent-to-treat (ITT) patients (11 out of 14) treated with 60mg selinexor achieved ≥35% reduction in spleen volume (SVR35) at week 24, and continued to remain in radiographic response as of the August 1, 2023 data cut-off date. In addition, 58% of the ITT patients (7 out of 12) who achieved symptom improvement of ≥ 50% (TSS50) at week 24 also remained in response as of the data cut-off. In general, early cytokine reduction at week 4 was associated with spleen volume reduction at week 24, was sustained until the end of treatment, and is a potential sign of disease modification.

- 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 (MM) progressing after T-cell immunotherapies, potentially adding to the growing body of evidence that selinexor has the potential to show meaningful benefit in combination with MM therapies with differing mechanisms of action; the study of selinexor/mezigdomide enables further evaluation of selinexor's role in maintaining an optimal T-cell environment.

XPOVIO Commercial Performance

- Achieved U.S. net product revenue for the year ended December 31, 2023 of $112 million, compared to

$120 million for the year ended December 31, 2022. U.S. net product revenue for the fourth quarter of 2023 was $25 million, compared to $31 million for the fourth quarter of 2022. Although demand for XPOVIO continued its growth in the community setting in 2023, it was adversely impacted in the academic setting due to increased competition in the later-lines.

- Continued progress in shifting selinexor use into earlier lines of therapy, with patient mix approaching 70% in the second to fourth lines in 2023 versus 55% in 2022[1].

- XPOVIO net product revenue was adversely impacted year-over-year by increased utilization of the KaryForward Patient Assistance Program (PAP), due to MM foundation closures[2], contributing to ~10% of total demand in 2023 as compared to ~5% in 2022, leading to an estimated impact of ~$6 million. 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 in 2023.

Intellectual Property

- The U.S. Patent and Trademark Office 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.

Anticipated Catalysts and Operational Objectives in 2024 and 2025

- Present updated exploratory subgroup analysis results in patients with *TP53* wild-type EC from the Phase 3 SIENDO trial in 2024.

- Complete enrollment in pivotal XPORT-EC-042 Phase 3 trial in *TP53* wild-type EC in 2H 2024 and report top-line results in 1H 2025.

- Report updated results from the Phase 1 trial of selinexor in combination with ruxolitinib in patients with treatment-naïve MF in 2024.

- Report preliminary results from the Phase 2 trial evaluating the efficacy and safety of selinexor monotherapy in subjects with JAK inhibitor-naïve MF and moderate thrombocytopenia in 2H 2024.

- Report top-line results from pivotal Phase 3 trial of selinexor in combination with ruxolitinib in treatment-naïve MF in 2H 2025.

- Publish and present efficacy and safety data on selinexor 40mg in combination with pomalidomide and dexamethasone from ongoing STOMP/028 Phase 2 trials in patients with MM in 2024.

- Report additional data on selinexor's impact on T-cell fitness and potential combinability with multiple agents pre- or post-T-cell therapy in patients with MM in 2024.

- Complete enrollment in pivotal Phase 3 trial evaluating an oral combination of 40mg selinexor, pomalidomide and dexamethasone in patients with previously treated MM in 2H 2024 and report top-line results in 1H 2025.

- 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.

2024 Financial Outlook

Based on its current operating plans, Karyopharm expects the following for full year 2024:

- Total revenue to be in the range of $140 million to $160 million. Total revenue consists of U.S. XPOVIO net product revenue and license, royalty and milestone revenue earned from partners.

- U.S. XPOVIO net product revenue to be in the range of $100 million to $120 million.

- R&D and SG&A expenses to be in the range of $260 million to $280 million, which includes approximately $20 million to $25 million of estimated non-cash stock-based compensation expense.

- The Company expects that its existing cash, cash equivalents and investments, and the revenue it expects to generate from XPOVIO net product sales, as well as revenue generated from its license agreements, will be sufficient to fund its planned operations into late 2025.

Full Year and Fourth Quarter 2023 Financial Results

Total revenue: Total revenue for the fourth quarter of 2023 was $33.7 million, compared to $33.6 million for the fourth quarter of 2022. Total revenue for the year ended December 31, 2023 was $146.0 million, compared to $157.1 million for the year ended December 31, 2022.

Net product revenue: Net product revenue for the fourth quarter of 2023 was $25.1 million, compared to $31.1 million for the fourth quarter of 2022. Net product revenue for the year ended December 31, 2023 was $112.0 million, compared to $120.4 million for the year ended December 31, 2022.

License and other revenue: License and other revenue for the fourth quarter of 2023 was $8.7 million, compared to $2.5 million for the fourth quarter of 2022. License and other revenue for the year ended December 31, 2023 was $34.0 million, compared to $36.6 million for the year ended December 31, 2022.

Cost of sales: Cost of sales for the fourth quarter of 2023 was $1.5 million, compared to $1.9 million for the fourth quarter of 2022. Cost of sales for the year ended December 31, 2023 was $4.9 million, compared to $5.2 million for the year ended December 31, 2022. Cost of sales reflects the costs of XPOVIO units sold and third-party royalties on net product revenue.

R&D expenses: R&D expenses for the fourth quarter of 2023 were $39.4 million, compared to $30.9 million for the fourth quarter of 2022. R&D expenses for the year ended December 31, 2023 were $138.8 million, compared to $148.7 million for the year ended December 31, 2022. The decrease in R&D expenses in 2023 compared to 2022 was primarily due to a decrease in personnel costs and stock-based compensation attributable to a reduction in headcount and contractors, including severance-related expenses incurred in 2022. These decreases were partially offset by an increase in clinical trial and related costs primarily due to the advancement of the Company's three pivotal Phase 3 trials and the timing of purchases of comparator drug used in the Company's clinical trials.

SG&A expenses: SG&A expenses for the fourth quarter of 2023 were $30.7 million, compared to $34.6 million for the fourth quarter of 2022. SG&A expenses for the year ended December 31, 2023 were $131.9 million, compared to $145.4 million for the year ended December 31, 2022. The decrease in SG&A expenses in 2023 compared to 2022 was primarily due to a decrease in stock-based compensation because of severance-related expenses incurred in 2022.

Interest expense: Interest expense for the fourth quarter of 2023 was $6.2 million, compared to $5.9 million for the fourth quarter of 2022. Interest expense for the year ended December 31, 2023 was $23.8 million, compared to $25.0 million for the year ended December 31, 2022.

Net loss: Karyopharm reported a net loss of $41.8 million, or $0.36 per basic and diluted share, for the fourth quarter of 2023, compared to a net loss of $38.5 million, or $0.43 per basic and diluted share, for the fourth quarter of 2022. Net loss includes non-cash stock-based compensation expense of $5.2 million and $6.2 million for the fourth quarters of 2023 and 2022, respectively. Karyopharm reported a net loss of $143.1 million, or $1.25 per basic and diluted share, for the year ended December 31, 2023, compared to a net loss of $165.3 million, or $2.02 per basic and diluted share, for the year ended December 31, 2022. Net loss includes non-cash stock-based compensation expense of $21.7 million and $35.4 million for the years ended December 31, 2023 and 2022, respectively.

Cash position: Cash, cash equivalents, restricted cash and investments as of December 31, 2023 totaled $192.4 million, compared to $279.7 million as of December 31, 2022.

Conference Call Information

Karyopharm will host a conference call today, February 29, 2024, at 8:00 a.m. Eastern Time, to discuss the fourth quarter and full year 2023 financial results and the financial outlook for 2024 and to provide other business updates. 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 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, South Korea, Israel, Singapore, Hong Kong, Mainland China, Australia, Canada, Taiwan and Macau 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 (≥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 a growing number of ex-U.S. territories and countries, including Europe, the United Kingdom, China, South Korea, Israel, Singapore, Hong Kong, Mainland China, Australia, Canada, Taiwan and Macau, and is marketed in those areas by Karyopharm's global partners. Karyopharm has a focused pipeline targeting multiple high unmet need cancer indications, including in multiple myeloma, endometrial cancer 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 Karyopharm's guidance on its 2024 total revenue, 2024 U.S. net product revenue and 2024 R&D and SG&A expenses; Karyopharm's expected cash runway; expectations with respect to commercialization efforts; the ability of selinexor to treat patients with multiple myeloma, endometrial cancer, myelofibrosis, diffuse large B-cell lymphoma, 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 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; 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.

References:

[1] Based on Komodo claims data analysis, accessed in November 2023

[2] Four multiple myeloma foundations provide financial support to Medicare patients with multiple myeloma

KARYOPHARM THERAPEUTICS INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(unaudited)
(in thousands, except per share amounts)

	Three Months Ended December 31,		Years Ended December 31,	
	2023	**2022**	**2023**	**2022**
Revenues:				
Product revenue, net	$ 25,056	$ 31,126	$ 112,011	$ 120,445
License and other revenue	8,691	2,454	34,022	36,629
Total revenue	33,747	33,580	146,033	157,074
Operating expenses:				
Cost of sales	1,486	1,868	4,942	5,213
Research and development	39,381	30,932	138,750	148,662
Selling, general and administrative	30,688	34,649	131,881	145,401
Total operating expenses	71,555	67,449	275,573	299,276
Loss from operations	(37,808)	(33,869)	(129,540)	(142,202)
Other income (expense):				
Interest income	2,520	1,334	10,943	2,359
Interest expense	(6,208)	(5,885)	(23,823)	(24,996)
Other expense, net	(211)	(13)	(356)	(83)
Total other expense, net	(3,899)	(4,564)	(13,236)	(22,720)
Loss before income taxes	(41,707)	(38,433)	(142,776)	(164,922)
Income tax provision	(130)	(73)	(323)	(369)
Net loss	$ (41,837)	$ (38,506)	$ (143,099)	$ (165,291)
Net loss per share—basic and diluted	$ (0.36)	$ (0.43)	$ (1.25)	$ (2.02)
Weighted-average number of common shares outstanding used in net loss per share—basic and diluted	114,778	89,934	114,221	81,871

KARYOPHARM THERAPEUTICS INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(unaudited)
(in thousands)

	December 31, 2023	December 31, 2022

Assets		
Cash, cash equivalents and investments	$ 191,443	$ 277,967
Restricted cash	961	1,697
Accounts receivable	26,962	47,086
Other assets	21,072	31,422
Total assets	$ 240,438	$ 358,172
Liabilities and stockholders' deficit		
Convertible senior notes	$ 170,919	$ 170,105
Deferred royalty obligation	132,479	132,718
Other liabilities	73,246	72,005
Total liabilities	376,644	374,828
Total stockholders' deficit	(136,206)	(16,656)
Total liabilities and stockholders' deficit; 114,915 and 113,213 shares issued and outstanding at December 31, 2023 and December 31, 2022, respectively	$ 240,438	$ 358,172

SOURCE Karyopharm Therapeutics Inc.

For further information: Investors: Elhan Webb, CFA, Senior Vice President, Investor Relations, 617.658.0600, elhan.webb@karyopharm.com; Media: Stacy Nobles, Head of Corporate Communications, 617.658.0540, stacy.nobles@karyopharm.com

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https://investors.karyopharm.com/2024-02-29-Karyopharm-Reports-Fourth-Quarter-and-Full-Year-2023-Financial-Results-and-Highlights-Recent-Company-Progress