Karyopharm Reports Fourth Quarter and Full Year 2022 Financial Results and Highlights Recent Company Progress

-- Total Revenue of $157.1 Million and U.S. XPOVIO® (selinexor) Net Product Revenue of $120.4 Million for Full Year 2022, Meeting Company's Guidance --

-- Updated Results from the Phase 1 Study of Selinexor in Combination with Ruxolitinib in Patients with Treatment-Naïve Myelofibrosis and Interim Data from the Phase 2 Study Evaluating Eltanexor in Relapsed/Refractory Myelodysplastic Neoplasms Expected in 1H 2023 --

-- Company Provides Full Year 2023 Total Revenue Guidance of $160 Million to $175 Million, Including U.S. XPOVIO Net Product Revenue Guidance of $125 Million to $140 Million; Cash Runway to Late 2025 --

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

NEWTON, Mass., Feb. 15, 2023 /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, 2022. In addition, Karyopharm highlighted select corporate milestones and provided an overview of its key clinical development programs.

"In 2022, Karyopharm delivered strong financial performance with a 22% increase in U.S. XPOVIO net product revenue, coupled with significant progress across our clinical pipeline and the achievement of several key regulatory milestones. Importantly, we solidified our financial runway to late 2025, enabling us to be well positioned to deliver the next stages of the company's growth," said Richard Paulson, President and Chief Executive Officer of Karyopharm. "Moving forward in 2023, we are excited to advance our mid-late stage pipeline and anticipate multiple data catalysts and robust progress across our programs in multiple myeloma, endometrial cancer, myelofibrosis and myelodysplastic neoplasms. We are passionate in our pursuit to bring forward innovative treatments that address critical unmet needs and positively impact the lives of people living with cancer."

Fourth Quarter 2022 and Recent Highlights

XPOVIO Commercial Performance

- Achieved U.S. net product revenue for the year ended December 31, 2022 of $120.4 million, up 22% compared to $98.4 million for the year ended December 31, 2021. U.S. net product revenue for the fourth quarter of 2022 was $31.1 million, up 4% from the fourth quarter of 2021.
- Continued progress in shifting selinexor use into earlier lines of therapy, with strong growth in the community setting, offsetting increased pressure in the academic setting due to intensifying late-line competition and ongoing trials.

R&D Highlights

- Initiated pivotal Phase 3 study of selinexor as a maintenance therapy following systemic therapy in patients with *TP53* wild-type advanced or recurrent endometrial cancer. Entered into a global collaboration with Foundation Medicine, Inc., a pioneer in molecular profiling for cancer, to develop FoundationOne®CDx, a *TP53* wild-type companion diagnostic for selinexor.
- Presented encouraging preliminary data from the Phase 1 study (XPORT-MF-034) evaluating selinexor in combination with ruxolitinib in patients with treatment-naïve myelofibrosis (MF) at the American Society of Hematology 2022 Annual Meeting. Initial data from the study were also presented at the European Hematology Association 2022 Hybrid Congress and the American Society of Clinical Oncology 2022 Annual Meeting.
- Orphan medicinal product designation granted by the European Commission for selinexor for the treatment of MF.

Corporate and Business Highlights

- Completed a $165 million private placement of common stock to new and existing shareholders, extending cash runway into late 2025.

Anticipated Near-Term Catalysts and Operational Objectives in 2023

- Continue to grow the Company's commercial foundation in the competitive multiple myeloma marketplace, driving increased XPOVIO sales.
- Additional global launches of selinexor by partners in ex-U.S. territories.
- Present data supporting optimization of selinexor dose in multiple myeloma and other key programs.
- Continue to generate data demonstrating selinexor's efficacy, combinability and tolerability in patients with multiple myeloma.
- Report interim data from the Phase 2 study evaluating eltanexor in relapsed/refractory myelodysplastic neoplasms in 1H 2023.
- Report updated results from the Phase 1 study of selinexor in combination with ruxolitinib in patients with treatment-naïve MF in 1H 2023. Initiate pivotal Phase 3 study in front-line MF in 1H 2023, subject to regulatory feedback.
- Present updated subgroup analysis results in patients with *TP53* wild-type endometrial cancer from the SIENDO study of selinexor versus placebo as maintenance therapy after first-line chemotherapy for advanced or recurrent endometrial cancer at a medical conference in 2023.
- Further exploration of biomarker subsets to identify patient populations who may best respond to SINE compounds.

2023 Financial Outlook

Based on its current operating plans, Karyopharm expects the following for full year 2023:

- Total revenue to be in the range of $160 million to $175 million. Total revenue consists of U.S. XPOVIO net product revenue and license, royalty and milestone revenue earned from our partners.
- U.S XPOVIO net product revenue to be in the range of $125 million to $140 million.
- Non-GAAP R&D and SG&A expenses, which exclude stock-based compensation expense, to be in the range of $260 million to $280 million. Karyopharm has not reconciled the full year 2023 outlook for non-GAAP R&D and SG&A expenses to full year 2023 outlook for GAAP R&D and SG&A expenses because Karyopharm cannot reliably predict without unreasonable efforts the timing or amount of the factors that substantially contribute to the projection of stock compensation expense, which is excluded from the full year 2023 outlook for non-GAAP R&D and SG&A expenses.
- The Company expects that its existing cash, cash equivalents and investments, and the revenue it expects to generate from XPOVIO 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 2022 Financial Results

Total revenue: Total revenue for the fourth quarter of 2022 was $33.6 million, compared to $126.3 million for the fourth quarter of 2021. Total revenue for the year ended December 31, 2022, was $157.1 million, compared to $209.8 million for the year ended December 31, 2021.

Net product revenue: Net product revenue for the fourth quarter of 2022 was $31.1 million, up 4% compared to $29.8 million for the fourth quarter of 2021. Net product revenue for the year ended December 31, 2022, was $120.4 million, up 22% compared to $98.4 million for the year ended December 31, 2021.

License and other revenue: License and other revenue for the fourth quarter of 2022 was $2.5 million, compared to $96.5 million for the fourth quarter of 2021. License and other revenue for the year ended December 31, 2022 was $36.6 million, compared to $111.4 million for the year ended December 31, 2021. This decrease in license and other revenue in both the fourth quarter and full year 2022 was primarily driven by $75.0 million of revenue recognized in the fourth quarter of 2021 related to the upfront payment that Karyopharm received from the Menarini Group in connection with execution of a license agreement in December 2021.

Cost of sales: Cost of sales for the fourth quarter of 2022 was $1.9 million, compared to $0.7 million for the fourth quarter of 2021. Cost of sales for the year ended December 31, 2022 was $5.2 million, compared to $3.4 million for the year ended December 31, 2021. Cost of sales reflects the costs of XPOVIO units sold and third-party royalties on net product revenue.

Research and development (R&D) expenses: R&D expenses for the fourth quarter of 2022 were $30.9 million, compared to $44.0 million for the fourth quarter of 2021. R&D expenses for the year ended December 31, 2022 were $148.7 million, compared to $160.8 million for the year ended December 31, 2021. The decrease in R&D expenses in 2022 compared to 2021 was primarily attributable to decreased clinical trial and related costs in 2022 due to the prioritization of the Company's core programs and the purchase of certain assets in 2021, partially offset by an increase in personnel costs and stock-based compensation, largely due to severance-related expenses incurred in 2022 in connection with the departure of certain executive officers.

Selling, general and administrative (SG&A) expenses: SG&A expenses for both the fourth quarters of 2022 and 2021 were $34.6 million. SG&A expenses for the year ended December 31, 2022 were $145.4 million, compared to $143.8 million for the year ended December 31, 2021. The slight increase in SG&A expenses compared to the prior year was due primarily to an increase in personnel costs and stock-based compensation, including severance-related expenses incurred in 2022 in connection with the departure of our former chief executive officer, partially offset by decreased consulting and professional fees.

Interest expense: Interest expense for the fourth quarter of 2022 was $5.9 million, compared to $7.9 million for the fourth quarter of 2021. Interest expense for the year ended December 31, 2022 was $25.0 million, compared to $26.0 million for the year ended December 31, 2021.

Net income (loss): Karyopharm reported net loss of $38.5 million, or $0.43 per basic and diluted share, for the fourth quarter of 2022, compared to a net income of $38.7 million, or $0.51 per basic and $0.46 per diluted share, for the fourth quarter of 2021. Net income (loss) includes non-cash stock-based compensation expense of $6.2 million and $6.9 million for the fourth quarters of 2022 and 2021, respectively. Karyopharm reported a net loss of $165.3 million, or $2.02 per basic and diluted share, for the year ended December 31, 2022, compared to a net loss of $124.1 million, or $1.65 per basic and diluted share, for the year ended December 31, 2021. Net loss includes non-cash stock-based compensation expense of $35.4 million and $29.8 million for the years ended December 31, 2022 and 2021, respectively.

Cash position: Cash, cash equivalents, restricted cash and investments as of December 31, 2022 totaled $279.7 million, compared to $235.6 million as of December 31, 2021.

Non-GAAP Financial Information

Karyopharm uses a non-GAAP financial measure, non-GAAP R&D and SG&A expenses, to provide operating expense guidance. Non-GAAP R&D and SG&A expenses exclude stock-based compensation expense. Karyopharm believes this non-GAAP financial measure is useful to investors because it provides greater transparency regarding Karyopharm's operating performance as it excludes non-cash stock compensation expense. This non-GAAP financial measure should not be considered a substitute or an alternative to GAAP R&D and SG&A expenses and should not be considered a measure of Karyopharm's liquidity. Instead, non-GAAP R&D and SG&A expenses should only be used to supplement an understanding of Karyopharm's operating results as reported under GAAP.

Conference Call Information

Karyopharm will host a conference call today, February 15, 2023, at 8:00 a.m. Eastern Time, to discuss the fourth quarter and full year 2022 financial results and the financial outlook for 2023 and to provide other business highlights. To access the conference call, 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 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, 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 (≥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 Karyopharm's guidance on its 2023 total revenue, 2023 U.S. net product revenue and 2023 non-GAAP R&D and SG&A expenses; Karyopharm's 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 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, which was filed with the Securities and Exchange Commission (SEC) on November 3, 2022, 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.

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

	Three Months Ended December 31,		Year Ended December 31,	
	2022	2021	2022	2021
Revenues:				
Product revenue, net	$ 31,126	$ 29,803	$ 120,445	$ 98,436
License and other revenue	2,454	96,466	36,629	111,383
Total revenues	33,580	126,269	157,074	209,819
Operating expenses:				
Cost of sales	1,868	742	5,213	3,402
Research and development	30,932	44,003	148,662	160,842
Selling, general and administrative	34,649	34,562	145,401	143,846
Total operating expenses	67,449	79,307	299,276	308,090
(Loss) income from operations	(33,869)	46,962	(142,202)	(98,271)
Other income (expense):				
Interest income	1,334	55	2,359	582
Interest expense	(5,885)	(7,940)	(24,996)	(26,046)
Other expense, net	(13)	(478)	(83)	(85)
Total other expense, net	(4,564)	(8,363)	(22,720)	(25,549)
(Loss) income before income taxes	(38,433)	38,599	(164,922)	(123,820)
Income tax (provision) benefit	(73)	121	(369)	(268)
Net (loss) income	$ (38,506)	$ 38,720	$ (165,291)	$ (124,088)
Net (loss) income per basic common share	$ (0.43)	$ 0.51	$ (2.02)	$ (1.65)
Weighted-average number of basic common shares	89,934	75,671	81,871	75,218
Net (loss) income per diluted common share	$ (0.43)	$ 0.46	$ (2.02)	$ (1.65)
Weighted-average number of diluted common shares	89,934	86,875	81,871	75,218

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

	December 31, 2022	December 31, 2021
Assets		
Cash, cash equivalents and investments	$ 277,967	$ 228,615
Restricted cash	1,697	6,986
Accounts receivable	47,086	22,497
Other assets	31,422	47,207
Total assets	$ 358,172	$ 305,305
Liabilities and stockholders' deficit		
Convertible senior notes	$ 170,105	$ 169,293
Deferred royalty obligation	132,718	132,998
Other liabilities	72,005	82,687
Total liabilities	374,828	384,978
Total stockholders' deficit	(16,656)	(79,673)
Total liabilities and stockholders' deficit; 113,213 and 75,746 shares issued and outstanding at December 31, 2022 and December 31, 2021, respectively	$ 358,172	$ 305,305

SOURCE Karyopharm Therapeutics Inc.

For further information: Investors: Elhan Webb, CFA, Senior Vice President, Investor Relations, 617.658.0600 | elhan.webb@karyopharm.com, or Media: Sarah Connors, Vice President, Corporate Communications, 617.658.0600 | sarah.connors@karyopharm.com

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Financial-Results-and-Highlights-Recent-Company-Progress