Karyopharm and Menarini Group Enter into Exclusive License Agreement to Commercialize NEXPOVIO® (selinexor) in Europe and Other Key Global Territories

Menarini Group Obtains Exclusive Rights to Commercialize NEXPOVIO for the Treatment of Hematologic and Solid Tumor Oncology Indications in Europe (including the United Kingdom), Latin America and Other Key Countries
Karyopharm to Receive $75 Million Upfront, then Eligible to Receive Up to $202.5 Million in Future Milestones, Plus Tiered, Double-digit Royalties on Net Sales

NEWTON, Mass. and FLORENCE, Italy, Dec. 21, 2021 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, and the Menarini Group, ("Menarini"), a privately-held, leading international pharmaceutical company, today announced their entry into an exclusive licensing agreement whereby Menarini will commercialize NEXPOVIO, Karyopharm's first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound, in Europe and other key global territories.

Under the terms of the agreement, Menarini received exclusive rights to commercialize NEXPOVIO for the treatment of oncology indications in the European Union and other European countries (including the United Kingdom), Latin America and other key countries. In exchange, Karyopharm will receive an upfront payment of $75 million (USD) in 2021 and is eligible to receive up to an additional $202.5 million in future milestones, plus tiered double-digit royalties on net sales of NEXPOVIO in the licensed territories.

"Menarini is a global pharmaceutical company, with a strong heritage and footprint in Europe and an unwavering commitment to patients, that is dedicated to innovation and bringing new treatment options in oncology. Menarini is an ideal partner to maximize selinexor's potential to have a positive impact on the treatment of cancer in Europe, Latin America and other key countries and this transaction marks an important step forward toward that goal," said Richard Paulson, President and Chief Executive Officer of Karyopharm. "With a shared vision on the potential of selinexor and Menarini's commercialization expertise, this agreement aligns our two companies with the common goal of expanding the number of patients who can access NEXPOVIO in these important global territories."

"We are delighted to partner with Karyopharm to provide NEXPOVIO in Europe, Latin America and other key countries in the world," said Elcin Barker Ergun, Chief Executive Officer of the Menarini Group. "Patients suffering from multiple myeloma continuously need different options as resistance develops to first line therapies and the unique mechanism of action of selinexor makes it an ideal partner as a backbone therapy in second line and beyond. The potential further expansion of NEXPOVIO in solid tumors, such as in endometrial cancers, where limited options exist, underline the wide potential of selinexor in playing a role in cancer treatments aligning well with our mission of providing therapies that can prolong patient lives."

NEXPOVIO has received conditional marketing authorization from the European Commission in combination with dexamethasone for the treatment of multiple myeloma in adult patients who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, two

immunomodulatory agents, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy. The European Medicines Agency (EMA) has validated the Marketing Authorization Application (MAA) for NEXPOVIO in combination with Velcade® (bortezomib) and low-dose dexamethasone for the treatment of multiple myeloma following at least one prior therapy. The MAA will be reviewed by the Committee for Medicinal Products for Human Use (CHMP), which will issue an opinion to the European Commission regarding the potential approval for the expanded indication. This review is expected to be completed during the first half of 2022.

About NEXPOVIO® (selinexor)

NEXPOVIO, which is marketed as XPOVIO in the U.S., is a first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound. NEXPOVIO functions by selectively binding to and inhibiting the nuclear export protein exportin 1 (XPO1, also called CRM1). NEXPOVIO blocks the nuclear export of tumor suppressor, growth regulatory and anti-inflammatory proteins, leading to accumulation of these proteins in the nucleus and enhancing their anti-cancer activity in the cell. The forced nuclear retention of these proteins can counteract a multitude of the oncogenic pathways that, unchecked, allow cancer cells with severe DNA damage to continue to grow and divide in an unrestrained fashion. NEXPOVIO (selinexor) has been granted conditional marketing authorization by the European Commission in combination with dexamethasone for the treatment of multiple myeloma in adult patients who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, two immunomodulatory agents, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

Therapeutic indication for NEXPOVIO in the EU as well as The EEA Countries of Iceland, Liechtenstein and Norway

NEXPOVIO is indicated in combination with dexamethasone for the treatment of multiple myeloma in adult patients who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, two immunomodulatory agents and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

IMPORTANT SAFETY INFORMATION

Contraindications: Hypersensitivity to selinexor.

Special warnings and precautions for use:

Recommended concomitant treatments
Patients should be advised to maintain adequate fluid and caloric intake throughout treatment. Intravenous hydration should be considered for patients at risk of dehydration.
Prophylactic concomitant treatment with a 5-HT3 antagonist and/or other anti-nausea agents should be provided prior to and during treatment with NEXPOVIO.

Haematology
Patients should have their complete blood counts (CBC) assessed at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two months of treatment.

Thrombocytopenia:
Thrombocytopenic events (thrombocytopenia and platelet count decreased) were frequently reported in adult patients receiving selinexor, which can be severe (Grade 3/4). Patients should be monitored for signs and symptoms of bleeding and evaluated promptly.

Neutropenia:

Severe neutropenia (Grade 3/4) has been reported with selinexor.
Patients with neutropenia should be monitored for signs of infection and evaluated promptly.

Gastrointestinal toxicity:
Nausea, vomiting, diarrhoea, which sometimes can be severe and may require the use of anti-emetic and anti-diarrhoeal medicinal products.

Weight loss and anorexia:
Patients should have their body weight, nutritional status and volume checked at baseline, during treatment, and as clinically indicated. Monitoring should be more frequent during the first two months of treatment.

Confusional state and dizziness:
Patients should be instructed to avoid situations where dizziness or confusional state may be a problem and to not take other medicinal products that may cause dizziness or confusional state without adequate medical advice. Patients should be advised not to drive or operate heavy machinery until symptoms resolve.

Hyponatraemia:
Patients should have their sodium levels checked at baseline, during treatment, and as clinically indicated. Monitoring should be more frequent during the first two months of treatment.

Tumour lysis syndrome (TLS):
TLS has been reported in patients receiving therapy with selinexor. patients at a high risk for TLS should be monitored closely. Treat TLS promptly in accordance with institutional guidelines.

Fertility, pregnancy and lactation
Women of childbearing potential/contraception in males and females:
Women of childbearing potential and male adult patients of reproductive potential should be advised to use effective contraceptive measures or abstain from sexual intercourse while being treated with selinexor and for at least 1 week following the last dose of selinexor.

Pregnancy:
There are no data from the use of selinexor in pregnant women. Selinexor is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breast-feeding:
It is unknown whether selinexor or its metabolites are excreted in human milk. A risk to breast-fed children cannot be excluded. Breast-feeding should be discontinued during treatment with selinexor and for 1 week after the last dose.

Undesirable effects
Summary of the safety profile
The most frequent adverse reactions (≥30%) of selinexor in combination with dexamethasone were nausea, thrombocytopenia, fatigue, anaemia, decreased appetite, decreased weight, diarrhoea, vomiting, hyponatraemia, neutropenia and leukopenia.

The most commonly reported serious adverse reactions (≥3%) were pneumonia, sepsis, thrombocytopenia, acute kidney injury, and anaemia.

Description of selected adverse reactions
Infections: Infection was the most common non-haematological toxicity. Upper respiratory tract infection and pneumonia were the most commonly reported infections with 25% of reported infections being serious and fatal infections occurring in 3% of treated adult patients.

Elderly population
Patients 75 years and older had a higher incidence of discontinuation due to an adverse reaction, higher incidence of serious adverse reactions, and higher incidence of fatal adverse reactions.

Reporting of suspected adverse reactions
Reporting of suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

Please see NEXPOVIO Summary of Product Characteristics and European Public Assessment Report at https://ec.europa.eu/health/documents/community-register/html/h1537.htm

About Karyopharm Therapeutics

Karyopharm Therapeutics Inc. (NASDAQ: KPTI) is a commercial-stage pharmaceutical company pioneering novel cancer therapies and dedicated to the discovery, development, and commercialization of first-in-class drugs directed against nuclear export for the treatment of cancer and other diseases. Karyopharm's Selective Inhibitor of Nuclear Export (SINE) compounds function by binding with and inhibiting the nuclear export protein XPO1 (or CRM1). Karyopharm's lead compound, XPOVIO® (selinexor), is approved in the U.S. in multiple hematologic malignancy indications, including in combination with Velcade® (bortezomib) and dexamethasone for the treatment of adult patients with multiple myeloma after at least one prior therapy, in combination with dexamethasone for the treatment of adult patients with heavily pretreated multiple myeloma and as a monotherapy for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma. NEXPOVIO® (selinexor) has also been granted conditional marketing authorization in combination with dexamethasone for adult patients with heavily pretreated multiple myeloma by the European Commission. In addition to single-agent and combination activity against a variety of human cancers, SINE compounds have also shown biological activity in models of neurodegeneration, inflammation, autoimmune disease, certain viruses and wound-healing. Karyopharm has several investigational programs in clinical or preclinical development. For more information, please visit www.karyopharm.com.

About Menarini Group

The Menarini Group is a leading international pharmaceutical and diagnostics company, with a turnover of $4.2 billion and over 17,000 employees. Menarini is focused on therapeutic areas with high unmet needs with products for oncology, cardiology, pneumology, gastroenterology, infectious diseases, diabetology, inflammation, and analgesia. With 18 production sites and 10 Research and Development centers, Menarini's products are available in 140 countries worldwide.

Menarini has a deep commitment for developing treatments addressing oncological and hematologic diseases. Menarini actively develops Elzonris (marketed in US and Europe for BPDCN) for multiple hematologic malignancies, including AML, CMML and myelofibrosis, and elacestrant and felezenexor for oncology as well. Additionally, the FDA recently granted MEN1703 an orphan drug designation for AML. For further information, please visit www.menarini.com.

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 potential to receive milestone and royalty payments under the license agreement with Menarini, the success of Karyopharm's arrangement with Menarini and the parties' ability to work effectively together, the timing of

submissions to regulatory authorities, Karyopharm's expectations and plans relating to XPOVIO for the treatment of hematologic malignancies or certain solid tumors; the expected design of the Company's clinical trials; and the therapeutic potential of and potential clinical development plans for Karyopharm's drug candidates, especially selinexor. Such statements are subject to numerous important factors, risks and uncertainties, many of which are beyond Karyopharm's control, that may cause actual events or results to differ materially from Karyopharm's current expectations. For example, there can be no guarantee that 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 ability of Karyopharm or Menarini to fully perform their respective obligations under the license agreement; 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 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 obtain and maintain requisite regulatory approvals and 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, 2021, which was filed with the Securities and Exchange Commission (SEC) on November 3, 2021, 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: Karyopharm Therapeutics, Investors: Argot Partners, Jason Finkelstein/Matthew DeYoung, 212.600.1902 | karyopharm@argotpartners.com; Media: 720 Strategies, Andrew Lee, andrew.lee@720strategies.com; Menarini Group: Valeria Speroni Cardi, Email: pressoffice@menarini.com

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Territories