Karyopharm and Menarini Group Announce Orphan Medicinal Product Designation from the European Commission for Selinexor for the Treatment of Myelofibrosis

NEWTON, Mass. and FLORENCE, Italy, Oct. 31, 2022 /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 that the European Commission (EC) has granted orphan medicinal product designation for selinexor for the treatment of myelofibrosis (MF). Selinexor was granted orphan drug designation in MF by the U. S. Food and Drug Administration (FDA) in May 2022. Karyopharm is currently evaluating selinexor, a first-in-class XP01 inhibitor, as monotherapy in patients with previously treated MF, and in combination with ruxolitinib in treatment-naïve patients. In December 2021, Karyopharm and Menarini entered into an exclusive licensing agreement whereby Menarini is responsible for commercializing all current and future indications of NEXPOVIO® in the European Economic Area, United Kingdom and Switzerland, CIS countries, Turkey and Latin America. Stemline Therapeutics B.V., a wholly owned subsidiary of Menarini, is leading all commercialization activities in Europe.

"We are very pleased to receive orphan medicinal product designation from the EC for selinexor for the treatment of myelofibrosis," said Reshma Rangwala, MD, PhD, Chief Medical Officer of Karyopharm. "Building on our recent orphan drug designation from the FDA, this recognition continues to reinforce the significant unmet need for a drug with a novel mechanism of action like selinexor for this devastating disease. Our clinical plans remain on track, and we look forward to the continued development of selinexor in MF."

"Myelofibrosis is a difficult-to-treat and complex disorder of the bone marrow with limited therapeutic options and we are committed to bringing novel treatments to patients through our collaboration with Karyopharm. We are excited about the potential to bring selinexor to myelofibrosis patients in Europe, pending positive study read-outs and regulatory approval," said Olivia del Puerto, MD LMS, Head of Medical Affairs Oncology - EMEA of Menarini.

About the EMA Orphan Designation

Orphan medicinal product designation in the European Union (EU) is granted by the European Commission which adopts the positive opinion issued by the European Medicines Agency (EMA) Committee for Orphan Medicinal Products. The EMA's orphan designation is available to companies developing treatments for life-threatening or chronically debilitating conditions that affect fewer than five in 10,000 persons in the EU. Medicines that meet the EMA's orphan designation criteria qualify for financial and regulatory incentives that include a 10-year period of marketing exclusivity in the EU after product approval, reduced fees and access to centralized marketing authorization.

About MF

MF is a rare type of bone marrow cancer that disrupts the body's normal production of blood cells. It causes extensive scarring of the bone marrow, leading to severe anemia that can cause weakness and fatigue. Bone marrow scarring can also cause a low number of platelets, which increases the risk of bleeding. MF affects males and females in equal numbers and can occur at any age, although it usually affects individuals 50 years old or older. According to the National Organization of Rare Diseases (NORD), the incidence is estimated to be 1.5 cases per 100,000 people in the United States and in Northern European countries, based on studies, the incidence is estimated to be 0.5 cases per 100,000 people.[1]

About NEXPOVIO® (selinexor)

NEXPOVIO®, which is marketed as XPOVIO® in the U.S., has been approved in the following oncology indications by the European Commission: (i) 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; and (ii) in combination with bortezomib and

dexamethasone for the treatment of adults with multiple myeloma who have received at least one prior therapy. The marketing authorization of NEXPOVIO is valid in the EU Member States as well as Iceland, Liechtenstein, Norway, and Northern Ireland. NEXPOVIO has been commercially available in Germany since October 1, 2022.

NEXPOVIO is a first-in-class, oral exportin 1 (XPO1) inhibitor. 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.

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

Please refer to local prescribing information where XPOVIO/NEXPOVIO is approved for full information.

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.

Cataract:
Selinexor can cause new onset or exacerbation of cataract. Ophthalmologic evaluation may be performed as clinically indicated. Cataract should be treated as per medical guidelines, including surgery if warranted.

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, diarrhea, 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 Authorisation 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.

About Karyopharm Therapeutics

Karyopharm Therapeutics Inc. (Nasdaq: KPTI) is a commercial-stage pharmaceutical company pioneering novel cancer therapies. Since its founding, Karyopharm has been the 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®), China, Singapore, Canada, Israel, South Korea, and Australia. Karyopharm has a focused pipeline targeting multiple high unmet need cancer indications, including in multiple myeloma, endometrial cancer, myelodysplastic syndromes 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.

About Menarini Group

The Menarini Group is a leading international pharmaceutical and diagnostics company, with a turnover of over $4 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 9 Research and Development centers, Menarini's products are available in 140 countries worldwide. For further information, please visit www.menarini.com 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 the ability of selinexor to treat

patients with multiple myeloma and expectations related to future clinical development and potential regulatory submissions of 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 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 June 30, 2022, which was filed with the Securities and Exchange Commission (SEC) on August 4, 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.

[1] NORD, Rare Disease Database, Primary Myelofibrosis, Accessed on 10/4/22, https://rarediseases.org/rare-diseases/primary-myelofibrosis/

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