

Karyopharm and Menarini Group Receive Full Marketing Authorisation from the European Commission for NEXPOVIO® (selinexor) for the Treatment of Patients with Multiple Myeloma After at Least One Prior Therapy

- Based on Results from Phase 3 BOSTON Study, Marketing Authorisation Expands Multiple Myeloma Indication -
- Approval Follows Positive Opinion by European Committee for Medicinal Products for Human Use (CHMP) in May 2022 -

NEWTON, Mass. and FLORENCE, Italy, July 21, 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 Marketing Authorisation for NEXPOVIO® (selinexor), a first-in-class, oral exportin 1 (XPO1) inhibitor, in combination with once-weekly bortezomib (Velcade®) and low-dose dexamethasone (SVd) for the treatment of adults with multiple myeloma who have received at least one prior therapy. With this approval for the extension of NEXPOVIO®'s indication in the European Union (EU), the conditional marketing authorisation is now converted to a full approval. The marketing authorisation, which marks the second indication for NEXPOVIO®, is valid in all 27 member states of the EU as well as Iceland, Liechtenstein, Norway, and Northern Ireland. Stemline Therapeutics B.V., a wholly owned subsidiary of the Menarini Group, will be responsible for all commercialization activities in Europe.

The approval follows a positive opinion granted in May 2022 by the CHMP based on results from the Phase 3 BOSTON study that demonstrated once-weekly SVd resulted in a statistically significant reduction in the risk of disease progression or death compared to standard twice-weekly bortezomib plus dexamethasone (Vd) regimen. The results from the BOSTON study were published in The Lancet (Grosicki, et al.) in November 2020.

"The European Commission's approval of an expanded use of NEXPOVIO® provides another option for patients with multiple myeloma who have relapsed, or become resistant to current treatment regimens," said Richard Paulson, President and Chief Executive Officer of Karyopharm. "Our decision to pursue approval for this patient population is indicative of our commitment to expand access to selinexor across the globe and we look forward to working closely with Menarini who will commercialize NEXPOVIO® in Europe."

"The approval of NEXPOVIO® marks an important step forward for patients in Europe where nearly 51,000 new cases of multiple myeloma are diagnosed each year and therapeutic options are limited," said Elcin Barker Ergun, Chief Executive Officer of Menarini. "We are committed to offering patients and physicians a valuable new treatment option and are working hard to make NEXPOVIO® available in different European countries as quickly as possible."

About the BOSTON study

The Marketing Authorisation is based upon the Phase 3 BOSTON (Bortezomib, Selinexor and Dexamethasone) study, which was a multi-center, randomized study ([NCT03110562](#)) that evaluated 402 adult patients with relapsed or refractory multiple myeloma who had received one to three prior lines of therapy. The study was designed to compare the efficacy, safety and certain health-related quality of life parameters of once-weekly SVd versus twice-weekly Vd. The primary endpoint of the study was progression-free survival and key secondary endpoints included overall response rate, rate of peripheral neuropathy, and others. To learn more about this study, please refer to Karyopharm and Menarini's [press release on the positive CHMP opinion](#) issued on May 20, 2022.

About Multiple Myeloma in Europe

Multiple myeloma is an incurable cancer with significant morbidity and the second most common hematologic malignancy. According to the World Health Organization, in 2020, there were approximately 51,000 new cases and 32,000 deaths from multiple myeloma in Europe¹. While the treatment of multiple myeloma has improved over the last 20 years, and overall survival has increased considerably, the disease remains incurable, and nearly all patients will eventually relapse and develop disease that is refractory to all approved anti-myeloma therapies. Therefore, there continues to be a high unmet medical need for new therapies, particularly those with novel mechanisms of action.

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 expanded NEXPOVIO® indication now allows adult patients with multiple myeloma to be treated in earlier lines of therapy. The indication for NEXPOVIO® is valid in the EU Member States as well as Iceland, Liechtenstein, Norway, and Northern Ireland. NEXPOVIO® is also approved in the UK under a Conditional Marketing Authorisation. The extension of indication in combination with bortezomib and dexamethasone for the treatment of adults with multiple myeloma who have received at least one prior therapy is currently under review by Medicines and Healthcare Products Regulatory Agency.

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>

UNITED STATES 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 ($\geq 30\%$) 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 ($\geq 3\%$) 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](https://twitter.com/Karyopharm) and [LinkedIn](https://www.linkedin.com/company/karyopharm).

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.

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 adult patients with multiple myeloma, the commercial launch of NEXPOVIO® in Europe, 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 March 31, 2022, which was filed with the Securities and Exchange Commission (SEC) on May 5, 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.

References

¹ World Health Organization. 2020. <https://gco.iarc.fr/today/data/factsheets/cancers/35-Multiple-myeloma-fact-sheet.pdf>

SOURCE Karyopharm Therapeutics Inc.

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