

Karyopharm Announces Clinical Trial Collaboration with Bristol Myers Squibb to Evaluate Novel CELMoD™ Agent CC- 92480 Mezigdomide in Combination with Selinexor in Patients with Relapsed/Refractory Multiple Myeloma

— *Phase 1b/2 Trial Will Investigate Mezigdomide in Combination with Selinexor in Patients with Relapsed/Refractory Multiple Myeloma Progressing after T-cell Immunotherapies* —

— *Expected to be Initiated 1H 2024* —

NEWTON, Mass., Oct. 30, 2023 [/PRNewswire/](#) -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced that it has entered into a clinical trial collaboration and supply agreement with [Bristol-Myers Squibb](#) (NYSE: BMY) to evaluate the company's proprietary investigational cereblon E3 ligase modulator (CELMoD™) agent mezigdomide in combination with Karyopharm's selinexor, an approved first-in-class inhibitor of Exportin 1 (XPO1), plus dexamethasone in patients with relapsed/refractory multiple myeloma.

This trial will evaluate mezigdomide in combination with selinexor doses of either 40mg or 60mg plus dexamethasone in patients who have prior exposure to immunomodulatory (IMiD®) drug agents, proteasome inhibitors, and anti-CD38 monoclonal antibody treatment. All patients must have received at least two prior lines of therapy, and either have progressed after or are not eligible to receive CAR-T or bispecific antibody treatment.

"This is an important collaboration with Bristol Myers Squibb to explore this novel and entirely oral combination in patients who have progressed following T-cell engaging therapy. This trial will also evaluate mezigdomide-selinexor plus dexamethasone in patients with relapsed/refractory multiple myeloma who need an effective alternative to T-cell therapies," said Richard Paulson, MBA, President and Chief Executive Officer of Karyopharm. "Pre-clinical studies with selinexor and mezigdomide post T-cell mediated therapies provide a scientific rationale for this novel combination to potentially prevent/reverse T-cell exhaustion and improve outcomes for more of these patients. We look forward to initiating the trial in the first half of 2024."

"Despite multiple treatment advances, there is a growing need for new combinations, particularly those that are all-oral, accessible and that have novel mechanisms to help treat patients with relapsed and refractory multiple myeloma," said Paul Richardson, M.D., the RJ Corman Professor of Medicine, Dana Farber Cancer Institute, and senior investigator of the study. "Pre-clinical data suggests the combination of a selective inhibitor of nuclear export (SINE), such as selinexor, with potent cereblon E3 ligase modulators, such as mezigdomide, may spare T-cell function while showing potential activity against resistant myeloma. This particular combination represents an innovative and promising approach to treating relapsed and refractory multiple myeloma with the convenience of an all-oral approach. We look forward to learning more about its potential in triple-class exposed patients, as well as in those who've experienced [anti-]BCMA and T-cell directed treatment failure."

The primary endpoints of this trial are to assess the objective response rate (ORR) and the clinical benefit rate (CBR). Key secondary endpoints include progression-free survival (PFS), overall survival (OS) and duration of response (DOR). In addition, the trial will evaluate dynamic changes in T-cell populations and activity as patients undergo treatment. Under the terms of the agreement with Bristol Myers Squibb, Karyopharm will sponsor the trial as a new arm of Karyopharm's Phase 1b/2 STOMP trial and Bristol Myers Squibb will supply the study's clinical drug mezigdomide.

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 various indications in a growing number of ex-U.S. territories and countries, including but not limited to the European Union, the United Kingdom, China, South Korea, Canada, Israel and Taiwan. XPOVIO and NEXPOVIO is marketed by Karyopharm's partners, Antengene, Menarini, Neopharm and FORUS, in China, South Korea, Singapore, Australia, Hong Kong, Germany, Austria, Israel and Canada.

Please refer to the local Prescribing Information for full details.

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

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 ($\geq 20\%$) 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 ($\geq 10\%$) 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 ($\geq 20\%$) 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 $\geq 20\%$) in patients with DLBCL, excluding laboratory abnormalities, are fatigue, nausea, diarrhea, appetite decrease, weight decrease, constipation, vomiting, and pyrexia. Grade 3–4 laboratory abnormalities ($\geq 15\%$) 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 Mezigdomide

Cereblon E3 ligase modulators (CELMoD™) are a class of oral immunomodulatory therapeutics that are designed to stimulate the immune system and directly kill cancer cells by inducing the degradation of tumor-promoting proteins. Bristol Myers Squibb is investigating a novel CELMoD™ agent, mezigdomide, for multiple myeloma that was intentionally designed to improve upon the demonstrated efficacy of the IMiD agents, along with manageable tolerability, ease of administration, and the potential to improve patient outcomes. Mezigdomide co-opts cereblon to rapidly induce degradation of target proteins Ikaros and Aiolos, thus inhibiting tumor cell proliferation, promoting tumor cell death, and inducing immune-stimulatory effects.

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](https://twitter.com/Karyopharm) and [LinkedIn](https://www.linkedin.com/company/karyopharm).

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, endometrial cancer and myelofibrosis; the benefits and results that may be achieved through the collaboration with BMS; and expectations related to the clinical development of selinexor 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 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; 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 June 30, 2023, which was filed with the Securities and Exchange Commission (SEC) on August 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.

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