Karyopharm Announces: FDA Considers the Effectiveness and Safety Technical Sections Complete to Support Conditional Approval for the New Animal Drug Application for Verdinexor (KPT-335) to Treat Lymphoma in Client Owned Dogs

NATICK, Mass., June 16, 2014 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company focused on the discovery and development of novel, first-in-class drugs directed against nuclear transport targets for the treatment of cancer and other major diseases, today announced that the U.S. Food and Drug Administration (FDA) Center for Veterinary Medicine (CVM) has found the effectiveness and safety technical sections complete to support conditional approval under a New Animal Drug Application (NADA) for Karyopharm's novel, oral Selective Inhibitor of Nuclear Transport (SINE) compound Verdinexor (KPT-335) for the treatment of canine lymphoma. The use of Verdinexor to treat canine lymphoma has been designated a "minor use" in accordance with the Minor Use Minor Species (MUMS) Act. This makes the product eligible for conditional approval similar to orphan drug/accelerated approvals used for submissions of human therapeutics.

The effectiveness and safety technical sections of the NADA for Verdinexor were submitted to the FDA as part of a phased review approach to approval. The FDA has now agreed that the data presented in these sections can support the conditional approval of Verdinexor for canine lymphoma. Karyopharm anticipates working with a marketing partner to complete the final major technical section for the NADA, which covers the commercial-scale manufacturing (CMC) of Verdinexor. As part of conditional marketing approval, the sponsor is required to conduct a full, often randomized, study, to confirm the activity of the conditionally approved agent within five years.

"FDA's confirmation that the effectiveness and safety sections of Verdinexor's NADA are now complete represents an important milestone towards the availability of a novel, orally bioavailable treatment for dogs with lymphoma," commented Cheryl London, D.V.M., Ph.D., Diplomate of the ACVIM (Oncology), Shackelford Professor of Veterinary Medicine at the Ohio State University College of Veterinary Medicine and Lead Investigator on the Phase 2 trial of Verdinexor that provided data to support the effectiveness part of the NADA. "There have been no new agents approved for the treatment of canine lymphoma in more than two decades. Current standard of care entails the use of chemotherapeutics, most of which require weekly intravenous administration. Many dog owners are not able to make the required hospital visits to veterinary specialists for injectable chemotherapy treatments and in some instances, are reluctant to pursue the use of cytotoxic chemotherapy due to potential side effects. Verdinexor is an easily administered oral therapy with a manageable side effect profile that provides an alternative approach to treating lymphoma by allowing owners to administer this agent to their dogs at home. The preliminary data suggest that treatment with Verdinexor can halt disease progression in the majority of the dogs, and in approximately one third of cases, it can induce tumor shrinkage. Importantly, Verdinexor has shown activity against both new and relapsed cases of lymphoma, and in both B and T cell subtypes of lymphoma. This will be further evaluated in a larger study following conditional approval of the NADA."

Following a Phase 1 dose escalation study, Verdinexor was tested in a Phase 2 study designed to meet requirements for conditional approval in companion dogs with B-cell or T-cell Non-Hodgkin's Lymphoma (NHL). The Phase 2 study was managed by Animal Clinical Investigation (ACI), conducted at ten ACI network clinics and academic institutions, and overseen by board certified veterinary medical oncologists at each site. Fifty-eight (58) pet dogs were enrolled in the study: 35 with newly diagnosed lymphoma and 23 with lymphoma at first relapse following standard injectable chemotherapy treatment. Of the 58 dogs, 42 had B-cell lymphoma, 14 had T-cell lymphoma and two had lymphoma of undetermined phenotype. Owners administered Verdinexor to their dogs two to three times per week by mouth after a meal at doses of 1.25-1.5 mg/kg. Response evaluation was based on objective measures per the Veterinary Cooperative Oncology Group (VCOG) standardized response criteria for peripheral lymphoma. Verdinexor was generally well tolerated with serious adverse events being uncommon. The most common side effect was reduced food intake, which was typically reversible with altered diet, the addition of low dose prednisone, and/or by alteration of Verdinexor dose or schedule. Single-agent Verdinexor induced an overall objective response rate of 34% (20/58 dogs) including 19 partial responses and

one complete response (in a dog with T-cell lymphoma). There was little evidence of cumulative toxicity in treated dogs. Approximately 20% of dogs enrolled in this study continued on single agent Verdinexor therapy for more than three months and approximately 15% of the dogs continued therapy for more than four months. A validated quality of life questionnaire was completed by owners of dogs enrolled into this study at each treatment visit. Importantly, Verdinexor was shown to have no negative impact on the quality of life of dogs treated in this study, supporting the notion that this therapy is well tolerated over long-term administration.

"We are very pleased that FDA has found Verdinexor to be safe and have a reasonable expectation of effectiveness for treating lymphoma in client owned dogs," stated Dr. Sharon Shacham, Karyopharm's Founder, President and CSO. "The diagnosis of cancer can be traumatic for dog owners and their families. Current standard of care treatment for dogs with lymphoma typically involves the use of injectable chemotherapies that require weekly office visits, often with a veterinary specialist. Verdinexor represents a novel oral therapy that can be given by owners at home, providing an alternative therapy that may allow many more dogs access to treatment for their lymphoma."

About Canine Lymphoma

Lymphoma is one of the most common cancers in dogs, and is rapidly fatal if untreated. Canine lymphoma is quite similar to human non-Hodgkin Lymphoma (NHL) and includes approximately 75% to 80% of B-cell derived tumors; the remainder are of T-cell or of undetermined origin. The majority of canine B-cell lymphomas are closely related to human diffuse large B-cell lymphoma (DLBCL), which is the most common type of human NHL and, like human DLBCL, is considered highly aggressive. Canine T-cell lymphoma is considered to be more challenging to treat than B-cell lymphoma (similar to the case in humans) and is often refractory to standard chemotherapeutics. Current therapeutic options for dogs with lymphoma include multi-agent intravenous chemotherapy protocols with steroids such as CHOP (cyclophosphamide, hydroxydaunorubicin, vincristine [Oncovin] and prednisone), high dose steroids alone, or palliative care. Chemotherapy combinations require administration under the care of veterinary specialists (typically a board certified Veterinary Medical Oncologist), frequent blood testing and follow up visits. While these combinations induce high response rates, more than 80% of treated dogs eventually relapse with median overall survival times ranging from 10 to 14 months. Many owners choose not to treat their dog with lymphoma given the need to travel to see a veterinary specialist for frequent office visits. Alternative treatments for this disease that would permit more dog owners access to therapy are thus needed, particularly given the lack of advances in disease management over the past two decades.

About the New Animal Drug Application (NADA)

Marketing authorization for a drug for veterinary use requires approval by the FDA's Center for Veterinary Medicine (CVM). The NADA for non-food animal applications includes four major technical sections: (i) Effectiveness (providing either "substantial evidence of effectiveness" toward full approval or a "reasonable expectation of effectiveness" for sponsors seeking conditional approval), (ii) Target Animal Safety, (iii) Environmental Impact (for which Verdinexor has received an exemption), and (iv) Chemistry, Manufacturing & Controls (CMC). These sections may be submitted as "rolling submissions," meaning that CVM will review each section independently. When each section is deemed complete, the Sponsor then files an administrative NADA for final conditional or full approval. Conditional approval under the MUMS designation requires that a separate confirmatory efficacy study be conducted within five years and also prohibits non-labelled use of the product during the conditional approval phase. Products with a MUMS designation have seven years of market exclusivity.

About Verdinexor (KPT-335)

Verdinexor (KPT-335) is a novel, oral Selective Inhibitor of Nuclear Export (SINE) compound being evaluated for the treatment of canine cancers, including lymphoma. Karyopharm's SINE compounds, including Selinexor (KPT-330) currently being tested in humans with advanced cancers, and verdinexor, inhibit the nuclear export function of Exportin-1 (XPO1 or CRM1). This inhibition prevents the export of tumor suppressor proteins and leads to their accumulation in the nucleus, which reinitiates and amplifies their natural apoptotic function. Nuclear localized tumor suppressor proteins detect cancer-associated DNA damage, leading to the selective apoptosis of cancer cells; normal cells, which do not have significant DNA damage, are spared.

About Karyopharm Therapeutics

Karyopharm Therapeutics Inc. (Nasdaq:KPTI) is a clinical-stage pharmaceutical company focused on the discovery and development of novel first-in-class drugs directed against nuclear transport targets for the treatment of cancer and other major diseases. Karyopharm's Selective Inhibitors of Nuclear Export (SINE) compounds function by binding with and inhibiting the nuclear export protein XPO1 (or CRM1). The inhibition of XPO1 by Karyopharm's lead drug candidate, Selinexor (KPT-330), a first-in-class, oral SINE compound, leads to

the accumulation of tumor suppressor proteins in the cell nucleus, which subsequently reinitiates and amplifies their tumor suppressor function. This is believed to lead to the selective induction of apoptosis in cancer cells, while largely sparing normal cells. SINE compounds have shown biological activity in models of cancer, autoimmune disease, certain viruses, and wound-healing. Karyopharm was founded by Dr. Sharon Shacham and is located in Natick, Massachusetts. For more information, please visit www.karyopharm.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 therapeutic potential of and potential clinical development plans for Karyopharm's drug candidates, including Verdinexor (KPT-335) and the related compound Selinexor (KPT-330), which is currently in Phase 1 and Phase 2 clinical trials in humans. Such statements are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from the company's current expectations. There can be no guarantee that any positive developments in 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: 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; Karyopharm's ability to obtain and maintain requisite regulatory approvals and to enroll patients in its clinical trials; unplanned cash requirements and expenditures; development of drug candidates by Karyopharm's competitors for diseases in which Karyopharm is currently developing its drug candidates; and Karyopharm's ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing. These and other risks are described under the caption "Risk Factors" in Karyopharm's Annual Report on Form 10-K for the year ended December 31, 2013, which is on file with the Securities and Exchange Commission (SEC), 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 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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