

Karyopharm Therapeutics Presents Clinical Data for Selinexor (KPT-330), a First-in-Class Selective Inhibitor of Nuclear Export (SINE), in Solid Tumors at the 2013 ASCO Annual Meeting

Karyopharm Therapeutics Presents Clinical Data for Selinexor (KPT-330), a First-in-Class Selective Inhibitor of Nuclear Export (SINE), in Solid Tumors at the 2013 ASCO Annual Meeting Natick, Mass. – June 2, 2013 – Karyopharm Therapeutics Inc., a leader in the new field of nuclear transport modulators, today announced the presentation of clinical data from an ongoing phase 1 clinical trial of its lead oral SINE selinexor (KPT-330) in patients with advanced solid tumors at the 2013 American Society of Clinical Oncology (ASCO) Annual Meeting being held in Chicago, IL. The data suggest that selinexor is generally safe and well tolerated as a single agent and exhibits the first signs of clinical efficacy in heavily pre-treated patients with advanced solid tumors even at low dose levels.

“We were pleased to present data on the sustained tolerability and durability of selinexor in our phase 1 dose escalation trial and to have achieved a durable partial response and several durable minor responses among patients with relapsed metastatic solid tumors who have exhausted available therapies,” said Karyopharm President and Head of Research and Development Sharon Shacham, Ph.D. “Based on the partial response in one patient and prolonged disease stabilization in seven additional patients as evidenced in this trial, we are eager to move into the dose expansion phase and look forward to initiating additional single agent and combination trials.”

In the phase 1 advanced solid tumor study presented at ASCO, 26 patients received oral selinexor (single agent) across seven dose levels (3 to 40 mg/m², 10 doses per 4-week cycle). One patient with colorectal cancer has achieved a partial response and six additional patients have stable disease lasting more than six cycles (24 weeks). Overall, about 50% of patients had stable disease on at least one radiographic evaluation after initiating selinexor therapy. The drug was well-tolerated at doses up to 30 mg/m² (MTD). Dose limiting toxicities at 40 mg/m² were grade 3 anorexia/dehydration and fatigue that resolved rapidly after interruption of therapy. The most common grade 3/4 adverse events were hyponatremia (14%), fatigue (11%), nausea (9%) and thrombocytopenia (9%). Selinexor demonstrated favorable pharmacokinetic parameters (C_{max} and AUC) that increased fairly linearly with the increasing doses, without affecting the half-life or clearance of the drug. Pharmacodynamic analyses demonstrated a significant rise (2-20 fold) in XPO1 mRNA levels in circulating leukocytes at doses ≥ 12 mg/m². In addition, tumor biopsy analyses confirmed selinexor-induced nuclear localization of tumor suppressor proteins supporting the anticipated mechanism of action of SINE.

Selinexor is an oral, small molecule SINE that induces cell death selectively in cancer cells through forced nuclear retention and activation of tumor suppressor proteins by blocking Exportin 1 (XPO1). Selinexor is being tested in both solid tumor and hematologic malignancies and is the first oral, small molecule XPO1 antagonist ever to be tested in humans.

About the Phase 1 Selinexor Trial

Data were reported from 26 patients treated in the dose escalation phase 1 clinical trial. The primary objectives of the phase 1 dose escalation trial were to determine the safety, tolerability and recommended phase 2 dose (RP2D) of orally administered selinexor. All patients entered the study with growing tumors having been treated with currently available therapies. Without effective therapy, the tumors will likely progress in four to six weeks and may be fatal. Patients were administered selinexor orally for 10 doses in a 28-day cycle and response evaluation was done with CT scans every two cycles, along with detailed pharmacokinetic and pharmacodynamic analyses and serial tumor biopsies. Stable disease or no evidence of tumor growth for more than four to eight weeks is evidence of anti-tumor activity. Additional patients with several different advanced relapsed solid tumors are being enrolled in a dose expansion at a dose of 30-35 mg/m².

About Karyopharm

Karyopharm Therapeutics Inc. is a clinical-stage pharmaceutical company leading the new field of nuclear transport modulators. Karyopharm's selective inhibitors of nuclear export (SINE) function by trapping multiple tumor suppressor proteins in the nucleus, resulting in anti-cancer activity across multiple tumor types. Karyopharm's lead oral SINE, selinexor (KPT-330), is in two Phase 1 clinical studies for advanced solid tumor and hematologic malignancies. The related oral SINE, verdinexor (KPT-335), is being tested in a pivotal study as an oral treatment for dogs with Non-Hodgkin's Lymphoma, one of the most common canine cancers. The Company is also testing SINEs in autoimmune, viral and dermatologic disorders. Karyopharm Therapeutics was founded by Drs. Sharon Shacham and Michael Kauffman and is located in Natick, Massachusetts.

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