# Karyopharm Therapeutics Initiates Two Phase 1 Trials with Oral KPT-330, the First Selective Inhibitor of Nuclear Export (SINE), in Patients with Advanced Cancers

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Karyopharm Therapeutics Inc., a leader in the new field of nuclear transport modulators, announced dosing of patients in the first-in-human clinical trials with KPT-330. KPT-330 is the first oral SINE CRM1 antagonist to enter human studies. SINEs specifically and irreversibly inhibit the nuclear export protein CRM1 (chromosome region maintenance protein 1), also called exportin 1 (XPO1). CRM1 is the exclusive mediator of nuclear export of p53, p73, pRb, FOXO, p21, p27, BRACA1, the endogenous inhibitor of Nuclear Factor κB (NF-κB) known as IκB, and other tumor suppressor and growth regulatory proteins. Nuclear export of these key proteins leads to their functional inactivation. Blockade of CRM1 leads to accumulation and activation of tumor suppressor and growth regulatory proteins in the nucleus, leading to potent and selective tumor cell apoptosis while sparing normal cells.

Patient dosing has been initiated in two phase 1 studies. The primary endpoints of both studies are to determine the safety and tolerability profile and the maximum tolerated dose of KPT-330 given orally 2-3 times per week. The first study includes patients with advanced solid tumors whose disease has progressed after at least one prior therapy for metastatic disease (NCT01607905). The second study includes patients with advanced hematologic malignancies including chronic lymphocytic leukemia, non-Hodgkin's lymphoma, multiple myeloma, and Waldenstrom's macroglobulinemia whose disease has relapsed after standard therapies (NCT01607892). Sharon Shacham, PhD, MBA, Karyopharm's Founder, Chief Scientific Officer, and head of research and development commented, "The initiation of these two Phase 1 trials with KPT-330 is a key milestone since the closing of our Series A funding and the initiation of our Company's operations in late 2010. This is the first oral SINE to ever enter human studies, and we are eager to assess the potential of our drug candidate across a wide variety of cancers."

The study is being conducted in the United States, Toronto, Canada, and Copenhagen, Denmark. NPM Pharma (Canada) is overseeing the trial on behalf of Karyopharm.

About Karyopharm Therapeutics Inc.
Karyopharm is a biopharmaceutical company leading the development of small molecule modulators of nuclear transport. The Company was founded by Drs. Sharon Shacham and Michael Kauffman in 2008. Karyopharm has raised approximately $34M since its inception and has won several grants/awards including a Biotech Investment Award by the Multiple Myeloma Research Foundation in 2010. Karyopharm's first program is directed towards the Selective Inhibition of Nuclear Export – its SINE program – targeting CRM1, the major nuclear export protein. SINE compounds, including KPT-330 and KPT-335, force the activation of the cell's key tumor suppressor proteins and anti-inflammatory pathways including p53, p21, pRB, FoxO, and IκB, a key cellular inhibitor of nuclear factor NF-κB. Karyopharm is currently evaluating

two oral SINE compounds in clinical trials. KPT-330 oral is being evaluated in patients with cancer, and KPT-335 oral is being studied in dogs with relapsed/refractory non-Hodgkin's Lymphomas. The Company is also evaluating the use of SINEs in autoimmune/inflammatory disorders, viral infections and dermatologic diseases. Karyopharm Therapeutics is located in Natick, Massachusetts.



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