

CanBas' Phase II Anti-Cancer Drug CBP501 Mechanisms Include Calmodulin Binding; CBS9106 Inhibits CRM1

Numazu City, Shizuoka, Japan - April 5, 2011 - CanBas Co., Ltd. presented new findings about mechanisms of action of two developmental anti-cancer agents at the American Association for Cancer Research (AACR) annual meeting, held in Orlando, FL, on April 2 - April 6, 2011.

New findings reported at AACR show that calmodulin inhibition plays an important role in the activity of CBP501 by sensitizing cancer cells to cisplatin or bleomycin. CBP501 was first described as a unique G2 checkpoint-directed agent. However, unlike G2 checkpoint inhibitors, CBP501 also enhances the G2/M accumulation induced by cisplatin or bleomycin at low dose and short exposure to tumor cells. Enhanced G2/M accumulation is the result of increased intracellular platinum concentration and binding to DNA. Calmodulin inhibition was identified as the mechanism of action of increased platinum concentration, and CBP501 was characterized as a G2 checkpoint abrogator with a unique calmodulin inhibiting activity with a broad therapeutic window ("CBP501-calmodulin binding contributes to sensitizing tumor cells to CDDP and BLM," AACR 2011 Annual Meeting, Abs. 2635).

CanBas also reported a series of experiments demonstrating that its novel anti-cancer compound, CBS9106, inhibits CRM1-dependent nuclear export and induces G1-arrest and apoptosis in a time- and dose-dependent manner in a broad spectrum of cancer cells including multiple myeloma. CBS9106 acts reversibly and reduces CRM1 protein without affecting mRNA expression level. Experimental results suggest that it acts on the CRM1 domain that includes the Cys-528 covalent binding site of the (toxic) CRM1 inhibitor, Leptomycin B, leading to proteasome-dependent CRM1 degradation. Oral administration of CBS9106 significantly suppressed tumor growth and prolonged reduction of CRM1 protein in tumor xenografts without causing significant body weight loss ("CBS9106 is a novel low toxic reversible oral CRM1 inhibitor with CRM1 degrading activity," AACR 2011 Annual Meeting, Abs. 658).

"We are excited by the new mechanism of action findings with CBP501. The addition of unique calmodulin inhibition activity suggests the development of a new class of anti-cancer drugs. CBS9106 demonstrates low toxicity and novel CRM1 inhibitory activity and is a promising candidate for progression into the clinic," said Takumi Kawabe, MD, PhD, CEO of CanBas.

About CBP501 and CBS9106

CBP501 is a synthetic peptide discovered using CanBas' proprietary phenotypic screen for G2 abrogation activity. CBP501 reduces phosphorylation of CDC25C on Ser216 and increases intracellular concentration of cisplatin. Randomized Phase II studies are ongoing in the US and other countries for first-line treatment

of late stage malignant pleural mesothelioma (MPM) and non-small cell lung cancer (NSCLC). CBS9106 is a preclinical stage, synthetic small molecule that demonstrates cancer cell-specific cytotoxicity, both alone and in synergy with certain DNA-damaging treatments, acting through inhibition and destabilization of CRM1.

About CanBas

CanBas is a publicly listed (Tokyo Stock Exchange: M-4575), clinical-stage biopharmaceutical company focused on the discovery and development of novel oncology drugs targeting the cell cycle. CanBas has developed a proprietary phenotypic screening platform, which has been used to identify a pipeline of novel oncology drug candidates, including CBP501 and CBS9106.

Source: [CanBas Co., Ltd.](#)

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