

CanBas' Phase II Anticancer Drug CBP501 Unique Calmodulin Binding Mechanism of Action Published in AACR Journal

Numazu, Shizuoka, Japan – August 24, 2011 - CanBas Co., Ltd. (CanBas) announces the publication of research findings demonstrating the contribution of a unique calmodulin binding mechanism of action (MOA) to the tumor sensitizing properties of the anticancer drug, **CBP501**.

CBP501 is a G2 checkpoint-directed agent that inhibits the actions of Chk1, Chk2, MAPKAP-K2 and C-Tak1. However, unlike other G2 checkpoint inhibitors, CBP501 also enhances cisplatin- or bleomycin-induced accumulation of tumor cells at the G2/M phase. Enhanced tumor cell accumulation at G2/M is the result of increased intracellular platinum concentration, which leads to increased binding of platinum to DNA.

A research group led by Dr. Takumi Kawabe, CEO of CanBas, concluded that calmodulin inhibition contributes to CBP501's sensitization of cancer cells to cisplatin and that this additional MOA might explain the observed clinical activity of the CBP501-cisplatin combination. The CBP501-cisplatin combination is currently undergoing randomized Phase II trials in the US and other countries for first-line treatment of late stage malignant pleural mesothelioma (MPM) and non-small cell lung cancer (NSCLC).

It is notable that CBP501 enhancement of tumor cell accumulation at the G2/M phase was induced by cisplatin or bleomycin (at low doses and short exposures), but not by radiation, doxorubicin or 5-fluorouracil. Studies of the CBP501-calmodulin interaction revealed a direct, high-affinity molecular interaction that is reversed by calcium ion (Ca⁺⁺).

Dr. Kawabe said, "Calmodulin binding and inhibition appears to be an important mechanism of action of CBP501 and may account for the significant effects we have observed in clinical trials. Although some calmodulin inhibitors behave similarly, they are far less potent than CBP501. We look forward to the near-term completion of both the MPM and NSCLC Phase II trials."

The research paper, "**CBP501-calmodulin binding contributes to sensitizing tumor cells to CDDP and BLM**," was published in *Molecular Cancer Therapeutics* (OnlineFirst August 10, 2011; doi: 10.1158/1535-7163.MCT-10-1139), which is a publication of the American Association of Cancer Research (AACR).

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. Using its proprietary phenotypic screening platform, CanBas has identified a pipeline of novel oncology drug candidates. The company's most advanced product, CBP501, is a synthetic peptide that was discovered in a phenotypic screen for G2 abrogation activity

and has been shown to increase intracellular concentration of cisplatin. CBP501 is undergoing randomized Phase II trials 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 specific DNA-damaging treatments, acting through inhibition and destabilization of CRM1.

Source: CanBas Co., Ltd.

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