

## **CBS9106 MoA Published in *Blood* - CanBas' Preclinical Anticancer Drug is a Novel Reversible Oral CRM1 Inhibitor with CRM1 Degrading Activity**

**Numazu, Shizuoka, Japan - August 24, 2011** - CanBas Co., Ltd. (CanBas) announces the publication of research findings indicating that CBS9106 is a novel reversible CRM1 inhibitor and a promising clinical candidate for the treatment of cancer.

Although CRM1 plays an important role in the nuclear export of cargo proteins bearing nuclear exporting signal sequences, the well-known CRM1 inhibitor, Leptomycin B (LMB), is highly toxic.

CanBas is in preclinical development with CBS9106, a synthetic small molecule which demonstrates cancer cell-specific cytotoxicity both alone and in synergy with specific DNA-damaging treatments, acting through inhibition and destabilization of CRM1.

A new study demonstrates that the novel compound, **CBS9106**, inhibits CRM1-dependent nuclear export, causing arrest of the cell cycle and inducing apoptosis in a time- and dose-dependent manner for a broad-spectrum of cancer cells, including multiple myeloma cells.

In this study, CBS9106 reduced CRM1 protein levels significantly without affecting CRM1 mRNA expression. The addition of bortezomib or LMB reversed this effect. Moreover, CBS9106-biotin allowed capture of CRM1 protein by streptavidin beads in competitive manner with LMB and vice versa. Mass spectrometric analysis found that CBS9106 reacts with a synthetic CRM1 peptide that contains Cys528, but not with a Cys528 mutant peptide. Oral administration of CBS9106 significantly suppressed tumor growth and prolonged survival in mice bearing tumor xenografts, without causing a significant loss in body weight. A reduced level of CRM1 protein was also observed in tumor xenografts isolated from mice treated with CBS9106.

Dr. Takumi Kawabe, CEO of CanBas and research leader of the new study, said, "These findings indicate great promise for CBS9106 as a drug candidate with the potential for inhibiting CRM1 without causing the toxic effects that preclude the clinical use of LMB in patients with cancer."

The research paper, "**CBS9106 is a novel reversible oral CRM1 inhibitor with CRM1 degrading activity**," was published in the journal, *Blood*. (2011 Aug 12. [Epub ahead of print]).

### **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.

### **Contact**

Takumi Kawabe, CEO  
CanBas Co., Ltd.  
CBS9106@canbas.co.jp

<http://www.canbas.co.jp/eng/>