

## Complete regression of ovarian cancer xenografts following treatment with the recombinant immunocytotoxic protein, VB6-845

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### ABSTRACT

VB6-845 is a recombinant fusion construct consisting of a tumor-targeting Fab linked to de-immunized Bouganin, a type 1 ribosome-inactivating protein (RIP). VB6-845 specifically targets the epithelial cell adhesion molecule (Ep-CAM) that is highly expressed on many different epithelial carcinomas, including ovarian cancer. Ovarian cancer is the fourth most common cause of cancer mortality in women. Advances in surgery and treatment modalities have improved survival, but prognosis remains poor with a five-year survival rate of about 30% indicating the need for more effective treatment. Immunohistochemistry (IHC) determined a high level of VB6-845 immunoreactivity in ovarian primary (>90%) and metastatic (90%) carcinomas. VB6-845 exhibited potent activity against the ovarian Ep-CAM positive cancer cell line, OVCAR-3 as determined using an MTS assay, with an IC<sub>50</sub> of 0.6 nM, (0.26 µg/mL). *In vivo* efficacy of VB6-845 was demonstrated in the OVCAR-3 subcutaneous implanted xenograft model in SCID mice. I.V. administration of 10 & 20 mg/kg of VB6-845 resulted in 100% survival as compared to 27% survival in the untreated group on Day 75. The majority of the mice (80%) dosed at 20 mg/kg were tumor free ( $p < 0.001$ ) at the end of the study. *In vivo* efficacy of VB6-845 also was demonstrated in the OVCAR-3 intraperitoneal (I.P.) implanted xenograft model in Balb/c *Nude* mice. I.P. administration of 10 mg/kg of VB6-845 resulted in 93% survival as compared to 0% in the untreated group on Day 84 ( $p < 0.0001$ ) and none of the treated mice had tumor masses or ascites. CA125 levels of mice treated with VB6-845 were not different from tumor-free mice ( $p = 0.9889$ ) whereas untreated mice had CA125 levels significantly higher than treated mice ( $p < 0.0001$ ). Efficacy also was demonstrated in another Ep-CAM positive MCF-7 model, whereas VB6-845 had negligible effect on the Ep-CAM negative A-375 model.