B7T3 (CD276) is an immune checkpoint in the B7 family of molecules, many of which interact with known checkpoint markers including CTLA4, PD-1 and CD28. B7T3 is also overexpressed in many solid cancers and its overexpression has been correlated with disease severity. Targeting B7T3 in cancer treatment can reduce cell proliferation, progression, and metastasis. Potent therapies target B7T3 designed with reduced off-tumor toxicity are expected to lead to improved therapeutic options and better clinical outcomes.

Nectin4 is a predictive marker for cancer diagnosis and is a validated therapeutic target. It is believed to play a mechanistic role in cancer metastasis and angiogenesis of several types of primary tumors, as well as being a general target for adenocarcinomas. Nectin4 expression has a significant correlation with tumor grade and stage associated to tumor progression. Next generation Nectin4 therapies offer the potential to improve patient survival.

RESULTS

• CAB B7T3 x CAB CD3 bispecific antibody binds to recombinant human B7T3 ECD and CD3 epsilon/delta heterodimer protein with higher affinity in conditions mimicking the tumor microenvironment pH compared to conditions mimicking the normal tissue pH (A)

• CAB B7T3 x CAB CD3 pH profile showed that the affinity to human CD3 and human B7T3 were higher in acidic tumor microenvironment pH (6.0-6.5), lower in physiological pH (7.4) (B)

• CAB B7T3 x CAB CD3 dose at 2mg/kg BIW x led to a complete tumor regression in a Detroit 562 MXen model, comparable to WT B7T3 x WT CD3 at the same dose (C)

CONCLUSIONS

• CAB B7T3 x CAB CD3 and CAB Nectin4 x CAB CD3 bispecific antibodies have increased binding under tumor conditions compared to normal conditions. The pH profile ELISA confirmed the differential affinity with the pH ranges from 6.0 to 7.4, which should translate to reduced on-target, off-tumor toxicity in non-human primates (studies in process).

• CAB B7T3 x CAB CD3 and CAB Nectin4 x CAB CD3 bispecific antibodies have similar efficacy in cancer cell line derived MXeno models in vivo compared to the non-CAB benchmark antibodies.

• The BioAtla CAB platform offers the potential to transform bispecific solid tumor therapies through the widening of the therapeutic index.