**ABSTRACT**

Ideal targets for antibody drug conjugates (ADCs) are highly and homogeneously expressed on tumor cells in a wide variety of tumor types and in a high proportion of patients. Such targets should also be efficient cellular internalizers and have limited expression on normal tissues. Unfortunately, targets that meet all these criteria are rare. ADCs are developed by linking a cytotoxic payload to tumor-targeting antibodies to exploit the dysregulation of tumor-protective mechanisms that is characteristic of most cancers. The Probody platform is designed to minimize interaction with healthy tissues, mitigate “off-target” toxicity regardless of expression outside the tumor, and greatly expand the number of potential ADC targets.

**EXPERIMENTAL DESIGN**

**Mouse Clinical Trial**

158 tumors from 198 patients

Enrollment of the mouse clinical trial (MCT) (Fig. 4)

Each mouse harbored one unique tumor derived from one patient, and the mice were treated with CX-2009. Tumors were not preselected for high CD166 expression. The untreated control group consisted of N greater than 3.

**RESULTS**

**CX-2009 induces tumor growth inhibition in majority of PDX models tested to date (Fig. 6)**

Percent tumor growth inhibition (TGI) is plotted for 129 PDX models tested with CX-2009. Percent TGI is determined by 100 x (final tumor volume of treated / final tumor volume of untreated). Post-treatment tumor volume is greater than 100% TGI is associated with tumor shrinkage in 9/19 (47%) high CD166 models. These data suggest high CD166 expression may identify patients most likely to respond.

**SAMPLE BREAKDOWN**

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<td>32</td>
<td>33</td>
</tr>
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</table>

**SUMMARY/CONCLUSIONS**

1) CX-2009 is a Probody drug conjugate targeting a novel target, ALCAM (CD166), which is highly expressed on a variety of different cancer subtypes.

2) CX-2009 anti-tumor activity is being evaluated in 198 PDX tumor models using a mouse clinical trial format and 5 mg/kg qw2x3 dosing-129 models (65%) have been dosed to date.

3) CX-2009 is broadly active in unselected PDX models using this short-term and limited dosing regimen.

4) CD166 mRNA level was associated with antitumor activity, with tumor shrinkage in 49/47 (100%) high CD166 models. These data suggest high CD166 expression may identify patients most likely to respond to CX-2009. Analysis of CD166 expression in these models by IHC is ongoing.

**ACKNOWLEDGEMENTS**

PDX models using a murine clinical trial format is performed in collaboration with South Texas Accelerated Research Therapeutics (START)