Axl is a TAM family receptor tyrosine kinase that has been implicated in the pathogenesis of many cancer types. The high level of expression on the cancer cell surface has made it an attractive target for antibody therapeutics. However, Axl is expressed on many normal tissues and has been implicated in wide ranging requisite biological processes including response of endothelial cells to vascular injury, hematopoiesis, and regulation of immune responses. This normal tissue expression may limit Axl as a target for antibody therapeutics.

CAB-Ab antibodies, and CAB-ADCs were active against Axl positive human tumor xenografts with tumor stasis observed at 1mg/kg weekly and tumor regressions observed at 1 mg/kg twice a week dose levels. A non-specific IgG-ADC showed minimal efficacy at the same dose levels. Single dose studies in cynomolgus macaques have demonstrated that CAB-Ab-ADC has reduced liver toxicity and immune system effects compared to Axl-ADCs that bind to Axl under normal conditions.

In conclusion, our data is consistent with our work on CAB-EGFR antibodies, and suggests that ADCs generated using the CAB technology provides biologics with increased therapeutic index. Specifically, the CAB-Axl-ADC is an excellent candidate for evaluation as a treatment for human cancers that are Axl positive.

**REFERENCES**

2. Lu Q and Lemke G. Science. 2001 Jul 13;293(5501):11

**RESULTS**

**CONCLUSIONS**

CAB-Axl-ADC that bind to Axl under tumor but not normal conditions have been generated.

CAB-Axl-ADC are efficacious in a pancreatic xenograft model.

CAB-Axl-Ab and CAB-Axl-ADC have increased serum concentration of Ab compared to affinity matched Axl-Ab and Axl-ADC.

CAB-Axl-ADC have reduced toxicity compared to affinity matched Axl-ADC and phenocopy liver and immune system effects found in TAM+ mice.

CAB-Axl-ADC have opportunity for increased therapeutic index.

**ABBREVIATIONS**

ADC: Antibody Drug Conjugate
AM: Affinity Matched
CAB: Conditionally Active Biologic
Axl: AXL Tyrosine Kinase
EGFR: Epidermal Growth Factor Receptor
TAM: Tyrosine Kinase Associated with Metastasis
TAM+: TAM expressing
Wt: Wild Type