**Background**

AGEN2373 is a CD137 agonist antibody designed to selectively enhance innate and adaptive immunity only in presence of Fcγ-receptors (FcγR).

**Tool building for modeling AGEN2373 responses in mice**

AGEN2373 versus its mouse surrogate desired key characteristics

**Epitope**

Fc format &

A: Fc hinge

B: A/I ratio

C: HUg1, 100 mg/kg

D: 

Validation of AGEN2373 true surrogate clone S3B1

**Objective**

AGEN2373 surrogate antibody, in combination with other CPMs, improve responses in cold tumor model mouse

**PD signatures reflect anti-mouse CD137 epitope/Fc format combinations mechanisms-of-action**

**Conclusions**

Preclinical efficacy and pharmacodynamic studies illustrated antibody critical CD137-epitope targeting and FcγR interactions that optimally promote innate and adaptive immune responses against solid tumors, while avoiding immune-related adverse events, especially liver inflammation observed for this antibody class.

AGEN2373 and an efficacy, epitope- and FcγR-matched surrogate antibody S3B1 exhibited select CD137 agonist activity only in the presence of FcγR.

AGEN2373 is an A/I domain 4-targeting antibody that drives intrinsically selective T cell expansion, NK cell activation, and Treg depletion but no systemic inflammation either in tumor or blood. In contrast, a CD137 domain targeting antibody 3H3 induced systemic immune cell activation.

Consistent with these findings, AGEN2373 monotherapy has shown clinical benefit in 4 patients (SD), and a favorable safety profile with no evidence of transaminides in 16 patients based on 1 mg/kg.

**Ephrin 1 study of AGEN2373 in combination with belinostat (ABT and PD-1 antibody) is planned.**