TPS3180 **Poster Session**

Phase 1 first-in-human clinical trial of AG01, a recombinant monoclonal antibody to progranulin/glycoprotein 88 (PGRN/GP88), to determine the safety, tolerability, pharmacokinetics, and preliminary anti-tumor response in subjects with advanced solid tumor malignancies.

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Background: GP88/PGRN is the largest member of the granulin/epithelin family. We demonstrated GP88's role as an autocrine growth & survival factor in breast cancer (BC): in ER+BC cells, GP88 stimulates proliferation & confers resistance to anti-estrogen therapy & aromatase inhibitors;GP88 is expressed in 80% of invasive ductal carcinomas & is negative in normal mammary tissue; GP88 tumor expression is a prognostic indicator of recurrence & death in BC pts; Elevated GP88 serum level in metastatic BC patients (pts) is associated with disease progression. PGRN/GP88 is overexpressed in several other solid tumors (non-small cell lung carcinoma, colorectal, bladder, ovarian, prostate & brain). In advanced NSCLC & prostate pts, elevated serum PGRN/GP88 have been found. These results make GP88/PGRN an ideal therapeutic & diagnostic target in BC and other solid tumors. An anti-human PGRN/GP88 monoclonal antibody (AG01) inhibiting PGRN/GP88 action was developed & expressed as recombinant antibody in CHO cells. Pharmacology, GMP manufacturing, formulation, stability studies & GLP toxicology studies in non-human primates were done. The IND application was cleared by the FDA to proceed with the first-in-human (FIH) AG01 study in adult subjects with advanced solid tumors. **Methods:** This IRB approved FIH study, will be conducted in 2 stages, dose escalation (1A) and dose expansion (1B). The 1A part is ongoing, with the 1 + (3+3) design. In the 1A part the AG01 is administered intravenously (IV) over 90 min. every 14 days +/- 1 day, 1 cycle = 28days, DLT assessments occur in the first 28 days of treatment. Five dose levels of AG01 & a -1 level are planned (level -1-0.5mg/kg, & 1mg/kg, 2mg/kg, 4mg/kg, 6mg/kg, 8 mg/kg). In 1A part of the study, initially an accelerated titration design (1pt/dose level) was utilized to guide dose progression & estimation of the maximum tolerated and/or administered dose (MTD/MAD). Eligibility criteria for 1A part include pts with advanced relapsed/refractory solid tumor malignancies who failed 1 or more standard of care (SOC) therapies or for whom no SOC treatment exists or is not tolerated, at least 1 RECIST1.1 measurable lesion, ECOG $<$ = 2, Life expectancy $>$ = 12wks, adequate organ & bone marrow function, willing to sign informed consent & follow study procedures. Primary objective (1A) is to determine the MTD and/or MAD of AG01. Secondary objectives: to determine the recommended phase 2 dose (RP2D), safety, tolerability, the PKs, immunogenicity & the preliminary anti-tumor activity of AG01. Exploratory objectives:todetermine PGRN/GP88 expression in tumor tissue & PGRN/ GP88 blood levels (A&G's IHC & ELISA test). This study is registered at NCT05627960. The study is supported by NCI grants NCI R44 CA224718 & CA162629. Clinical trial information: NCT05627960. Research Sponsor: National Cancer Institute; National Cancer Institute.