A PHASE 1, MULTICENTER, OPEN-LABEL, DOSE-ESCALATION, SAFETY, PHARMACODYNAMIC, PHARMACOKINETIC STUDY OF Q702 WITH A COHORT EXPANSION AT THE RP2D IN PATIENTS WITH ADVANCED SOLID TUMORS

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Background Q702 is an orally administrated novel Axl/Mer/CSF1R tyrosine kinase inhibitor that triggers the increase of IFN-γ production by CD8+ T cells, M1/M2 macrophage ratio, and tumor antigen presentation by MHC Class I.

Methods We initiated a first-in-human, multicenter, dose escalation study of Q702 in patients with advanced relapsed/refractory solid tumors. This study is designed to determine the MTD, DLTs, safety profile and the RP2D of single agent Q702. Secondary objectives include determining the PK profile of Q702 and the PD analysis. Dose escalation cohorts ranging from 4 to 240 mg (7 days on, 7 days off dosing schedule) follow an adaptive 3+3 design. Upon establishment of the RP2D, the dose expansion will initiate to further assess the safety and anti-tumor activity.

Results 30 patients with advanced solid tumors (median age 65y, range 32–81) with ECOG 0 or 1 and median of 5 prior lines (range 1–7) of therapies including immunotherapy, were enrolled. TRAEs occurred in ~15% of patients and included increased ALT (26.7%) and AST (23.3%), fatigue (23.3%) and dysgeusia (16.7%). The Grade 3 TRAEs observed were ALT increased (3.3%), anemia (6.7%), AST increased (3.3%), blood creatinine kinase (CK) increased (6.7%), and lymphocyte count decreased (6.7%). No Grade 4 TRAEs were observed. Other TRAEs included one case of Grade 2 somnolence and other Grade 1 neurological events. Despite not meeting MTD criteria, we decided to de-escalate as 240 mg was deemed not a feasible dose. Non-specific ocular findings were also observed. Preliminary PK data demonstrate the Q702 and primary metabolite exposure to be dose dependent. Of those 23 response-evaluable patients, 6 patients (26%) achieved stable disease across dose levels, 5 patients (22%) of which maintained stable disease for more than 16 weeks.

Conclusions Q702 is a novel Axl/Mer/CSF1R inhibitor with a manageable monotherapy safety profile up to 240 mg daily and early signals of anti-tumor activity. Dose optimization is ongoing. The asymptomatic and reversible AST, ALT and CK elevations appear to be among the most common AEs and are consistent with the mechanism of action. CSF1R inhibition is known to reduce Kupffer cells which are involved in ALT, AST and CK clearance that result in reversible liver enzyme elevations have been reported with other CSF1R targeted antibodies and small molecules.

Trial Registration NCT04648254

REFERENCE