

A Phase 1b/2a Study to Assess the Safety, Pharmacokinetics, and Preliminary Efficacy of TU2218, an oral TGF β R Serine/Threonine Kinase Inhibitor, Administered in Combination with Pembrolizumab in Patients with Advanced Solid Tumors.

TiumBio Co. Ltd



ONCOLOGY	Phase 1
Product Type	Chemical drug
Indication	Oncology
Target	Advanced solid tumors
MoA(Mechanism of Action)	TGF- β signaling inhibition
Competitiveness	<ul style="list-style-type: none"> • Unmet medical needs ✓ Immune checkpoint inhibitors (ICIs) have rapidly changed the treatment paradigm for multiple tumor types. Despite the unprecedented clinical benefit in some patients, unfortunately many patients do not respond with ICIs (primary resistance) and many patients with initial response will later develop acquired resistance. For this reason, there is an urgent need for the clinical development of novel agents for patients with primary and acquired ICIs resistance. ✓ High level of plasma TGF-β is significantly correlated with poor outcomes with approved ICIs. Poor clinical results for ALK5 inhibitors and bifunctional fusion protein targeting TGF-β and PD-L1 are also being reported in several clinical trials. Therefore, a novel therapeutic with superior efficacy differentiated from previous TGF-β modulators will demonstrate significant clinical outcomes in combination with ICIs. • Dual Inhibition of TGFβRI and VEGFR2 ✓ TU2218 is a highly potent, orally available inhibitor against ALK5 and VEGFR2 showing significant anti-tumor activities through immune activation in various tumor models. Immune tolerance by TGF-β and VEGF is inextricably related with poor outcomes of approved anti-PD-(L)1 therapy. Accordingly, a dual target for ALK5 and VEGFR2 via single or combination treatments can be an unequivocal tactic to tune tumor-microenvironment (TME) favorable to ICI, and to essentially overcome immune evasion against TGF-β- and VEGF-enriched tumors. ✓ Several in vitro results with human immune cells show TU2218 possesses potent anti-cancer immune activities through boosting T and NK immunity as well as blocking Treg activity, implicating the mechanism of overcoming immune tolerance and reversing immunosuppression in TME. ✓ In addition, TU2218 has synergistic anti-tumor activity combined with ICIs in numerous in vivo tumor model, showing the potential for novel combination options to develop promising therapeutics for patients with advanced cancer.
Development Stage	Phase I
Route of Administration	Oral