In vitro and in vivo Pharmacology

In vitro pharmacodynamic activity of TG-1701

Occupancy assay

Pathway inhibition

In vitro antiangiogenic activity of TG-1701

In vivo xenograft DOHH-2 model: Efficacy and PD study

In vivo xenograft OCI-17-10 model: comparison with alcalabrutinib

In the CIA mouse model, TG-1701 reduced arthritis clinical score

Conclusions

TG-1701 is a novel, specific and covalently bound BTK inhibitor.

Occupancy assays in vitro and in vivo suggest 95% occupancy can be reached using low dose in human dose escalation clinical trial.

TG-1701 inhibited the phosphorylation of BTK and other kinases downstream the BTK pathway, demonstrating a strong growth inhibitory activity against a set of lymphoma cell lines (data not shown) and inhibits chronic lymphocytic leukemia.

TG-1701 demonstrated similar antiangiogenic effects on the human and murine xenograft models.

PK profile allows for once-a-day dosing, TG-1701 is not a CYP inhibitor, and possesses a favorable profile for combination (data not shown).

In vivo, a single dose resolution has started in China.

TG-1701 will be tested in combination with several TI agents including rituximab and umbilizumab.