CB-708, an orally bioavailable small molecule inhibitor of CD73, immunosuppressant and anti-tumor activity

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Abstract

CD73 Generates Immunosuppressive Adenosine

CB-708 is a Potent CD73 Inhibitor in Full Human Plasma

CB-708 is Selective for CD73

CB-708 is More Efficacious than a Clinical CD73 Antibody

CB-708 Monotherapy Inhibits Established Tumors

CONCLUSIONS

CB-708 is an orally bioavailable and selective CD73 inhibitor with picomolar potency.

Adenosine-mediated suppression of CD4+ T-cell function and proliferation is reversed by CB-708.

CB-708 has good exposure in patients, is well-tolerated, and shows pharmacodynamic effect.

Anti-tumor single-agent activity of CB-708 is immunemediated.

CB-708 enhances the anti-tumor effect of checkpoint blockade and chemotherapy.

Preclinical studies show superior activity compared to a clinical CD73 antibody.

In GLP toxicology studies, no CB-708-related toxicity was identified at high exposures.