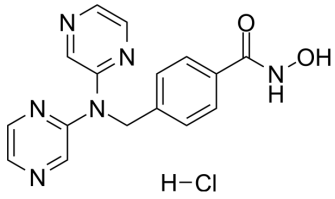
KA2507 monohydrochloride

Cat. No.:	HY-138799A
CAS No.:	2972712-63-1
Molecular Formula:	$C_{16}H_{15}ClN_6O_2$
Molecular Weight:	358.78
Target:	HDAC
Pathway:	Cell Cycle/DNA Damage; Epigenetics
Storage:	4°C, sealed storage, away from moisture and light * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



BIOLOGICAL ACTIVITY

Description

KA2507 hydrochloride is a potent and highly selective inhibitor of HDAC6 (IC_{50}=2.5 nM) with no significant toxicities. KA2507 hydrochloride shows antitumor efficacy and immune modulatory effects[1].

In Vitro

KA2507 hydrochloride does not inhibit the in vitro proliferation of mouse or human cancer cells at concentrations that are selective for HDAC6 inhibition. The anti-proliferative effects are only observed at high concentrations of KA2507 hydrochloride, which combines with the increased acetylation of histone H3 suggests that the anti-proliferative effects of KA2507 hydrochloride are attributable to off-target inhibition of class I HDAC as well as HDAC6[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

KA2507 hydrochloride (100-200 mg/kg; p.o.; daily; for 20 days) inhibits tumor growth in the syngeneic B16-F10 mouse melanoma model[1].

KA2507 hydrochloride also demonstrates antitumor efficacy in CT26 and MC38 colorectal cancer models[1].

Analysis of tumor samples also indicates modulation of biomarkers of antitumor immunity at efficacious dosing, with KA2507 hydrochloride administration resulting in reduced STAT3 activation (as measured by phospho-STAT3, an important suppressor of the antitumor immune response), reduced PD-L1 expression, and increased expression of MHC class I[1].

KA2507 hydrochloride exhibits poor oral bioavailability (mice 15%) and Cmax (mice 300 ng/mL) following oral administration (mice 200 mg/kg)[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male C57BL/6 mice, B16-F10 melanoma model[1]
Dosage:	100 mg/kg, 200 mg/kg,
Administration:	P.o.; once a day for 20 days
Result:	Inhibited tumor growth in the syngeneic B16-F10 mouse melanoma model.

Animal Model:	Male C57BL/6 mice, B16-F10 melanoma model[1]
Dosage:	200 mg/kg (Pharmacokinetic Analysis)
Administration:	Oral administration

Result:	Oral bioavailability (15%), Cmax (300 ng/mL).

REFERENCES

[1]. Tsimberidou AM, et al. Preclinical Development and First-in-Human Study of KA2507, a Selective and Potent Inhibitor of Histone Deacetylase 6, for Patients with Refractory Solid Tumors. Clin Cancer Res. 2021;27(13):3584-3594.

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