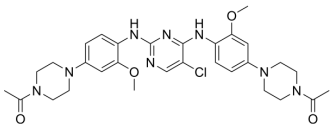
KRCA-0008

Cat. No.:	HY-12331
CAS No.:	1472795-20-2
Molecular Formula:	$C_{30}H_{37}ClN_8O_4$
Molecular Weight:	609.12
Target:	Ack1; Anaplastic lymphoma kinase (ALK); Apoptosis
Pathway:	Protein Tyrosine Kinase/RTK; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 230 mg/mL (377.59 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6417 mL	8.2086 mL	16.4171 mL
	5 mM	0.3283 mL	1.6417 mL	3.2834 mL
	10 mM	0.1642 mL	0.8209 mL	1.6417 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 5.75 mg/mL (9.44 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5.75 mg/mL (9.44 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.25 mg/mL (2.05 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

KRCA-0008 is a selective ALK/Ack1 inhibitor with IC_{50}s of 12 and 4 nM for ALK and Ack1, respectively. KRCA-0008 can be used for the research of cancer[1][2].

IC_{50} & Target

IC50: 12 nM (ALK), 4 nM (Ack1)[1]

In Vitro

KRCA-0008 (0-1000 μM) shows potency to ALK (wt), ALK L1196 M, ALK C1156Y, ALK F1174L, ALK R1275Q and insulin receptor with IC_{50}s of 12, 75, 4, 17, 17 and 210 nM, respectively[1].

KRCA-0008 (0-1000 nM; 4 h) inhibits ALK-dependent signaling pathways more potently than crizotinib[2].
KRCA-0008 (0-1000 nM; 72 h) induces cell apoptosis[2].
KRCA-0008 (0-100 nM; 48 h) affects cell cycle[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	H3122 and H1993 cell lines
Concentration:	200 nM
Incubation Time:	6 hours
Result:	Inhibited cell proliferation of H3122 and H1993 cells with IC_{50}s of 0.08 and 3.6 nM, respectively.

Cell Proliferation Assay[2]

Cell Line:	NPM-ALK-positive ALCL cell lines (Karpas-299 and SU-DHL-1) and U937 NPM ALK-negative lymphoma cell line
Concentration:	200 nM
Incubation Time:	72 hours
Result:	Inhibited proliferation of Karpas-299, SU-DHL-1 and U937 cells with GI_{50}s of 12 nM, 3 nM and 3.5 μM, respectively.

Western Blot Analysis[2]

Cell Line:	Karpas-299 and SU-DHL-1 cell lines
Concentration:	0, 10, 100 and 1000 nM
Incubation Time:	4 hours
Result:	Completely suppressed phosphorylation of ALK and its effectors at a dose of 100 nM in NPM-ALK-positive ALCL cells.

Apoptosis Analysis[2]

Cell Line:	SU-DHL-1 cell line
Concentration:	0-1 μM
Incubation Time:	72 hours
Result:	Dose-dependently increased cspase-3/7 activities and induced cell apoptosis.

Cell Cycle Analysis[2]

Cell Line:	Karpas-299 and SU-DHL-1 cell lines
Concentration:	0-100 nM
Incubation Time:	48 hours
Result:	Induced G0/G1 cell cycle arrest in ALCL cells expressing NPM-ALK.

In Vivo	KRCA-0008 (25 and 50 mg/kg; p.o. twice a day for two weeks) suppresses tumor growth in an ALK-positive Karpas-299

xenograft model[2].

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Animal Model:	NOD/SCID mice with Karpas-299 xenografts[2]
Dosage:	25 and 50 mg/kg
Administration:	Oral gavage; 25 and 50 mg/kg twice a day; for two weeks
Result:	Significantly inhibited tumor growth by inhibiting NPM-ALK phosphorylation without showing overt signs of toxicity or significant compound-related body weight loss.

CUSTOMER VALIDATION

- Chem Biol Interact. 2021 Nov 20;109747.

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REFERENCES

[1]. Hwang J, et al. KRCA-0008 suppresses ALK-positive anaplastic large-cell lymphoma growth. Invest New Drugs. 2020 Oct;38(5):1282-1291.

[2]. Park CH, et al. Novel bis-ortho-alkoxy-para-piperazinesubstituted-2,4-dianilinopyrimidines (KRCA-0008) as potent and selective ALK inhibitors for anticancer treatment. Bioorg Med Chem Lett. 2013 Nov 15;23(22):6192-6.

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