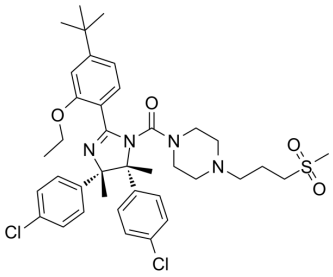
RG7112

Cat. No.:	HY-10959
CAS No.:	939981-39-2
Molecular Formula:	$C_{38}H_{48}Cl_2N_4O_4S$
Molecular Weight:	727.78
Target:	MDM-2/p53; E1/E2/E3 Enzyme
Pathway:	Apoptosis; Metabolic Enzyme/Protease
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 : 200 mg/mL (274.81 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.3740 mL	6.8702 mL	13.7404 mL
	5 mM	0.2748 mL	1.3740 mL	2.7481 mL
	10 mM	0.1374 mL	0.6870 mL	1.3740 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 10 mg/mL (13.74 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 10 mg/mL (13.74 mM); Clear solution
3. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 5 mg/mL (6.87 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (3.44 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

RG7112 is a potent, selective, first clinical, orally active and blood-brain barrier crossed MDM2-p53 inhibitor, with an IC_{50} of 18 nM and a K_D of 11 nM for binding to MDM2[1].

IC_{50} & Target

Kd: 11 nM (MDM2)[1]

In Vitro

RG7112 (0-5 μM) stabilizes wild-type p53 and induces p53 signaling in cancer cells. RG7112 effectively activates p53 functions in cancer cells[1][2].

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

Cell Proliferation Assay[2]

Cell Line:	SJSA1 osteosarcoma cells.
Concentration:	0-5 μM.
Incubation Time:	0-60 hours.
Result:	Dose-dependently inhibited the growth and killed SJSA1 osteosarcoma cells expressing high levels of MDM2 protein due to MDM2 gene amplification.

Cell Cycle Analysis[2]

Cell Line:	HCT116 and SJSA1 cells.
Concentration:	0-5 μM.
Incubation Time:	48 hours.
Result:	Induced a dose-dependent cell cycle block in G1 and G2/M phase and depletion of the S phase compartment.

In Vivo

RG7112 (25-200 mg/kg, single oral dose) activates p53 pathway and induces apoptosis in tumor cells in vivo[2].

RG7112 (100 mg/kg, gavage once per day, 5 days/week for 3 weeks) reduces tumor growth rate and increases survival in GBM models[3].

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

Animal Model:	Female Balb/c nude mice[2].
Dosage:	25-200 mg/kg.
Administration:	Orally, single dose.
Result:	At the highest dose level of RG7112 (200 mg/kg) only 1.2% (± 0.89 SD) of cells incorporated BrdU at 24 h post-dosing, vs. 14% (± 1.83 SD) of vehicle treated tumors.

Animal Model:	GBM cells were implanted into the brain of Athymic Nude mice (7 weeks old females, 10 animals/group)[3].
Dosage:	100 mg/kg.
Administration:	Oral gavage, once per day, 5 days/week for 3 weeks.
Result:	Reduced tumor growth rate and increases survival in heterotopic and orthotopic animal models bearing MDM2-amplified GBM.

CUSTOMER VALIDATION

- Adv Sci (Weinh). 2020 Aug 5;7(19):2001041.
- Nat Chem Biol. 2018 Feb;14(2):118-125.

- Clin Cancer Res. 2016 Mar 1;22(5):1185-96.
- EMBO J. 2019 Oct 15;38(20):e102096.
- Mater Sci Eng C Mater Biol Appl. 2020 Mar;108:110403.

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REFERENCES

[1]. Vu B, et al. Discovery of RG7112: A Small-Molecule MDM2 Inhibitor in Clinical Development. ACS Med Chem Lett. 2013 Apr 2;4(5):466-9.

[2]. Tovar C, et al. MDM2 small-molecule antagonist RG7112 activates p53 signaling and regresses human tumors in preclinical cancer models. Cancer Res. 2013 Apr 15;73(8):2587-97.

[3]. Verreault M, et al. Preclinical Efficacy of the MDM2 Inhibitor RG7112 in MDM2-Amplified and TP53 Wild-type Glioblastomas. Clin Cancer Res. 2016 Mar 1;22(5):1185-96.

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