产品名称：**RG7112**
产品别名：**RO5045337**

生物活性：		
Description	RG7112 is a potent, selective, first clinical, orally active and blood-brain barrier crossed MDM2-p53 inhibitor, with an IC50 of 18 nM and a KD 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].	
	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].	
	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.
	In Vitro: **DMSO : ≥ 100 mg/mL (137.40 mM)** **H_2O : < 0.1 mg/mL** (insoluble) * "≥" means soluble, but saturation unknown.	

<table>
<tr><td rowspan="2">Solvent&Solubility</td><td rowspan="4">Preparing Stock Solutions</td><td>Solvent / Mass / Concentration</td><td>1 mg</td><td>5 mg</td><td>10 mg</td></tr>
<tr><td>1 mM</td><td>1.3740 mL</td><td>6.8702 mL</td><td>13.7404 mL</td></tr>
<tr><td>5 mM</td><td>0.2748 mL</td><td>1.3740 mL</td><td>2.7481 mL</td></tr>
<tr><td>10 mM</td><td>0.1374 mL</td><td>0.6870 mL</td><td>1.3740 mL</td></tr>
<tr><td colspan="5">*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。
储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。
In Vivo:
请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：
——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶
1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline
Solubility: ≥ 10 mg/mL (13.74 mM); Clear solution
此方案可获得 ≥ 10 mg/mL (13.74 mM，饱和度未知) 的澄清溶液。
以 1 mL 工作液为例，取 100 μL 100.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。
2.请依序添加每种溶剂： 10% DMSO →90% corn oil
Solubility: ≥ 10 mg/mL (13.74 mM); Clear solution
此方案可获得 ≥ 10 mg/mL (13.74 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。
以 1 mL 工作液为例，取 100 μL 100.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。</td></tr>
<tr><td>References</td><td colspan="4">[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.</td></tr>
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