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产品名称: mTOR-IN-1
产品别名: mTOR-IN-1

生物活性:

Description	mTOR inhibitor-3 is a remarkably selective mTOR inhibitor with a K_i of 1.5 nM. mTOR inhibitor-3 suppresses mTORC1 and mTORC2 in cellular and in vivo pharmacokinetic (PK)/pharmacodynamic (PD) experiments.				
IC ₅₀ & Target	mTOR	mTORC1	mTORC2		
	1.5 nM (K _i)				
In Vitro	mTOR inhibitor-3 (Compound 12i) inhibits mTOR with a K_i of 1.5 nM, 500-fold selectivity over closely related PI3 kinases. mTOR inhibitor-3 inhibits NCI-PC3 and MCF7neo/Her2 cells proliferation with IC ₅₀ s of 150 nM and 57 nM, respectively[2].				
In Vivo	mTOR inhibitor-3 (Compound 8h) has high free plasma clearance in both mice (1818 mL/min/kg) and rats (1538 mL/min/kg in rat) [1]. mTOR inhibitor-3 (Compounds 12i) is selected for this study due to its potency, selectivity, and favorable mouse PK profile. Plasma levels of mTOR inhibitor-3 6 h following oral administration in PC3 tumor-bearing mice along with the fold decreases of phosphorylated mTORC1 and -2 substrates relative to time-matched vehicle controls. mTOR inhibitor-3 has moderate terminal elimination half-life ($t_{1/2}$ =1.7 h for mouse(1 mg/kg, iv)). mTOR inhibitor-3 achieves tumor stasis at the highest 200 mg/kg/day dose examined, which appears to also be approaching the limit of tolerability for this molecule[2].				
Solvent&Solubility	In Vitro: DMSO : 50 mg/mL (105.36 mM; Need ultrasonic)				
	Preparing Stock Solutions	Solvent Concentration Mass	1 mg	5 mg	10 mg
		1 mM	2.1072 mL	10.5361 mL	21.0722 mL
		5 mM	0.4214 mL	2.1072 mL	4.2144 mL
		10 mM	0.2107 mL	1.0536 mL	2.1072 mL
	*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→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (5.27 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.27 mM, 饱和度未知) 的澄清溶液。				



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	以 1 mL 工作液为例, 取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水溶液中, 混合均匀。 2. 请依序添加每种溶剂: 10% DMSO $\rightarrow$ 90% corn oil Solubility: $\geq$ 2.5 mg/mL (5.27 mM); Clear solution 此方案可获得 $\geq$ 2.5 mg/mL (5.27 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 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中, 混合均匀。
References	[1]. Pei Z, et al. Discovery and Biological Profiling of Potent and Selective mTOR Inhibitor GDC-0349. ACS Med Chem Lett. 2012 Nov 29;4(1):103-7. [2]. Koehler MF, et al. Potent, selective, and orally bioavailable inhibitors of the mammalian target of rapamycin kinase domain exhibiting single agent antiproliferative activity. J Med Chem. 2012 Dec 27;55(24):10958-71.
实验参考:	
Animal Administration	Mice^[2] Human prostate cancer NCI-PC3 cells are implanted subcutaneously into the right hind flanks of female NCR nude mice (5×10^6 cells in 100 μL of Hank's balanced salt solution). Tumors are monitored until they reach a mean tumor volume of approximately 500 mm³. Then similarly sized tumors are randomly assigned to groups (n=4). Compounds are formulated as suspensions in 0.5% methylcellulose/0.2% Tween 80 (MCT) and dosed orally at 25, 50, and 100 mg/kg (100 μL dose/25 g animal). Tumor and plasma samples are harvested at 1, 6, and 10 h postdose.
References	[1]. Pei Z, et al. Discovery and Biological Profiling of Potent and Selective mTOR Inhibitor GDC-0349. ACS Med Chem Lett. 2012 Nov 29;4(1):103-7. [2]. Koehler MF, et al. Potent, selective, and orally bioavailable inhibitors of the mammalian target of rapamycin kinase domain exhibiting single agent antiproliferative activity. J Med Chem. 2012 Dec 27;55(24):10958-71.