



上海源叶生物科技有限公司
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产品名称: **Gedatolisib (PF-05212384, PKI-587)**

CAS 号: **1197160-78-3**

产品货号: **S88003**

生物活性:

Description	Gedatolisib (PKI-587) 是一种高效的双重 PI3K α , PI3K γ 和 mTOR 抑制剂, IC ₅₀ 分别为 0.4 nM, 5.4 nM 和 1.6 nM。Gedatolisib 在 mTOR 复合物 mTORC1 和 mTORC2 中同样有效。				
IC ₅₀ & Target[1][3]	PI3K α	PI3K α -H1047R	PI3K α -E545K	PI3K γ	PI3K β
	0.4 nM (IC ₅₀)	0.6 nM (IC ₅₀)	0.6 nM (IC ₅₀)	5.4 nM (IC ₅₀)	6 nM (IC ₅₀)
	PI3K δ	mTOR	mTORC1	mTORC2	
	6 nM (IC ₅₀)	1.6 nM (IC ₅₀)			
Cellular Effect	Cell Line	Type	Value	Description	
	A-431	IC ₅₀	0.06 μ M	Antiproliferative activity against human A431 cells harboring wild type EGFR mutant assessed as reduction in cell viability incubated for 72 hrs by celltiter-glo assay	
	BaF3	IC ₅₀	0.1 μ M	Antiproliferative activity against mouse BaF3 cells harboring EGFR L858R/T790M/C797S mutant assessed as reduction in cell viability incubated for 72 hrs by celltiter-glo assay	
	CNE-2	IC ₅₀	0.2 μ M	Antiproliferative activity against human CNE-2 cells assessed as reduction in cell viability incubated for 48 hrs by MTT assay	
	HCT-116	IC ₅₀	0.51 μ M	Antiproliferative activity against human HCT-116 cells assessed as reduction in cell viability incubated for 48 hrs by MTT assay	
	HeLa	IC ₅₀	5.51 μ M	Antiproliferative activity against human HeLa cells assessed as reduction in cell viability incubated for 48 hrs by MTT assay	
	HepG2	IC ₅₀	14.76 μ M	Antiproliferative activity against human HepG2 cells assessed as reduction in cell viability incubated for 48 hrs by MTT assay	
	L02	IC ₅₀	27.33 μ M	Antiproliferative activity against human L02 cells assessed as reduction in cell viability incubated for 48 hrs by MTT assay	
	MCF7	IC ₅₀	0.37 μ M	Antiproliferative activity against human MCF7 cells assessed as reduction in cell viability incubated for 48 hrs by MTT assay	
	MDA-MB-231	IC ₅₀	1.08 μ M	Antiproliferative activity against human MDA-MB-231 cells assessed as reduction in cell viability incubated for 48 hrs by MTT assay	
	MDA-MB-361	IC ₅₀	< 10 nM	Inhibition of Akt S473 phosphorylation in human MDA-MB-361 cells by Western blotting	



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	<table><tr><td>MDA-MB-361</td><td>IC₅₀</td><td>3 nM</td><td>Growth inhibition of human MDA-MB-361 cells after 72 hrs</td></tr><tr><td>MDA-MB-361</td><td>IC₅₀</td><td>8 nM</td><td>Inhibition of Akt T308 phosphorylation in human MDA-MB-361 cells by Western blotting</td></tr><tr><td>NCI-H1975</td><td>IC₅₀</td><td>0.115 μM</td><td>Antiproliferative activity against human NCI-H1975 cells harboring EGFR L858R/T790M double mutant assessed as reduction in cell viability incubated for 72 hrs by celltiter-glo assay</td></tr><tr><td>PC-3</td><td>IC₅₀</td><td>11 nM</td><td>Growth inhibition of human PC3 cells after 72 hrs</td></tr><tr><td>Sf9</td><td>IC₅₀</td><td>0.4 nM</td><td>Inhibition of human PI3Kα expressed in Sf9 insect cells after 2 hrs by fluorescence polarization assay</td></tr><tr><td>Sf9</td><td>IC₅₀</td><td>11 nM</td><td>Inhibition of human PI3Kγ expressed in Sf9 insect cells after 2 hrs by fluorescence polarization assay</td></tr></table>	MDA-MB-361	IC ₅₀	3 nM	Growth inhibition of human MDA-MB-361 cells after 72 hrs	MDA-MB-361	IC ₅₀	8 nM	Inhibition of Akt T308 phosphorylation in human MDA-MB-361 cells by Western blotting	NCI-H1975	IC ₅₀	0.115 μM	Antiproliferative activity against human NCI-H1975 cells harboring EGFR L858R/T790M double mutant assessed as reduction in cell viability incubated for 72 hrs by celltiter-glo assay	PC-3	IC ₅₀	11 nM	Growth inhibition of human PC3 cells after 72 hrs	Sf9	IC ₅₀	0.4 nM	Inhibition of human PI3Kα expressed in Sf9 insect cells after 2 hrs by fluorescence polarization assay	Sf9	IC ₅₀	11 nM	Inhibition of human PI3Kγ expressed in Sf9 insect cells after 2 hrs by fluorescence polarization assay
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In Vitro	Gedatolisib (PKI-587) 在使用 MDA-361 和 PC3-MM2 细胞系的细胞生长抑制试验中表现出良好的效力, IC50 分别为 4.0 和 13.1 nM[1]。 Gedatolisib 可有效抑制 MDA-361 肿瘤细胞中 PI3K/mTOR 信号通路蛋白的磷酸化。Gedatolisib (0.03-3 μM; 4 小时) 阻止 Akt 在 Thr 308 处的磷酸化并在 30 nM 诱导裂解的 PARP[1]。 Western Blot Analysis[1] <table><tr><td>Cell Line:</td><td>MDA-361 tumor cells</td></tr><tr><td>Concentration:</td><td>0.03, 0.1, 0.3, 1, and 3 μM</td></tr><tr><td>Incubation Time:</td><td>4 hours</td></tr><tr><td>Result:</td><td>Prevented the phosphorylation of Akt (pAkt) at threonine 308 (T308; IC50=8 nM).</td></tr></table>	Cell Line:	MDA-361 tumor cells	Concentration:	0.03, 0.1, 0.3, 1, and 3 μM	Incubation Time:	4 hours	Result:	Prevented the phosphorylation of Akt (pAkt) at threonine 308 (T308; IC50=8 nM).																
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In Vivo	Gedatolisib (PKI-587; 在第 1、5、9 天以 20 mg/kg 静脉注射) 对小鼠 MDA-361 肿瘤表现出有效的抗肿瘤功效[1]。 由于高血浆清除率 (7 mL/min/kg) 和静脉注射后的大分布体积 (分别为 7.2 L/kg), Gedatolisib 表现出最终消除半衰期 (T1/2 14.4 h)。给药 (25 mg/kg) 雌性裸鼠[1]。 <table><tr><td>Animal Model:</td><td>Female nude mice bearing MDA-361 xenograft model[1].</td></tr><tr><td>Dosage:</td><td>20 mg/kg</td></tr><tr><td>Administration:</td><td>Administered i.v. at 20 mg/kg on an intermittent regimen (days 1, 5, 9).</td></tr><tr><td>Result:</td><td>Caused regression of large staged (~900 mm³) tumors.</td></tr><tr><td></td><td>The minimum efficacious dose (MED) was determined to be 3 mg/kg against MDA-361 tumors and maximum tolerated single dose (MTD) was determined to be 30 mg/kg.</td></tr></table>	Animal Model:	Female nude mice bearing MDA-361 xenograft model[1].	Dosage:	20 mg/kg	Administration:	Administered i.v. at 20 mg/kg on an intermittent regimen (days 1, 5, 9).	Result:	Caused regression of large staged (~900 mm³) tumors.		The minimum efficacious dose (MED) was determined to be 3 mg/kg against MDA-361 tumors and maximum tolerated single dose (MTD) was determined to be 30 mg/kg.														
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Solvent&Solubility	细胞实验: DMSO 中的溶解度 : 4 mg/mL (6.50 mM; 加热助溶; 吸湿的 DMSO 对产品的溶解度有显著影响, 请使用新开封的 DMSO) H2O 中的溶解度 : < 0.1 mg/mL (insoluble) <table><tr><td rowspan="2">Preparing</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>1.6241 mL</td><td>8.1204 mL</td><td>16.2409 mL</td></tr></table>	Preparing	Solvent / Mass Concentration	1 mg	5 mg	10 mg	1 mM	1.6241 mL	8.1204 mL	16.2409 mL															
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	Stock Solutions	5 mM	0.3248 mL	1.6241 mL	3.2482 mL
		10 mM	---	---	---
	*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℃, 6 months; -20℃, 1 month。-80℃ 储存时，请在 6 个月内使用，-20℃ 储存时，请在 1 个月内使用。				
参考文献	[1]. Venkatesan AM, et al. Bis(morpholino-1,3,5-triazine) derivatives: potent adenosine 5'-triphosphate competitive phosphatidylinositol-3-kinase/mammalian target of rapamycin inhibitors: discovery of compound 26 (PKI-587), a highly efficacious dual inhibitor. J Med Chem. 2010, 53(6), 2636-2645. [2]. Freitag H, et al. Inhibition of mTOR's Catalytic Site by PKI-587 Is a Promising Therapeutic Option for Gastroenteropancreatic Neuroendocrine Tumor Disease. Neuroendocrinology. 2017;105(1):90-104.				
完整储备液配制表：					
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。					
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可选溶剂	质量 溶剂体积 浓度	1 mg	5 mg	10 mg	25 mg
DMSO	1 mM	1.6241 mL	8.1204 mL	16.2409 mL	40.6022 mL
	5 mM	0.3248 mL	1.6241 mL	3.2482 mL	8.1204 mL