产品名称：**PI-103**
产品别名：**PI-103**

生物活性：

Description

PI-103 is a potent PI3K and mTOR inhibitor with IC50s of 8 nM, 88 nM, 48 nM, 150 nM, 20 nM, and 83 nM for p110α, p110β, p110δ, p110γ, mTORC1, and mTORC2. PI-103 also inhibits DNA-PK with an IC50 of 2 nM.

IC_{50} & Target

p110α	p110β	p110δ	p110γ	mTORC1	mTORC2
8 nM (IC_{50})	88 nM (IC_{50})	48 nM (IC_{50})	150 nM (IC_{50})	20 nM (IC_{50})	83 nM (IC_{50})
PI3KC2β	PI3KC2α	hsVPS34	DNA-PK	ATR	ATM
26 nM (IC_{50})	1 μM (IC_{50})	2.3 μM (IC_{50})	2 nM (IC_{50})	850 nM (IC_{50})	920 nM (IC_{50})
PI4KIIIβ					
50 μM (IC_{50})					

In Vitro

PI-103 exhibits antiproliferative properties in a panel of human cancer cell lines[1]. PI-103 is essentially cytostatic for cell lines and induced cell cycle arrest in the G1 phase. In blast cells, PI-103 inhibits leukemic proliferation, the clonogenicity of leukemic progenitors and induces mitochondrial apoptosis, especially in the compartment containing leukemic stem cells [2]. PI-103 potently inhibits both the rapamycin-sensitive (mTORC1, IC50=20 nM) and rapamycin-insensitive (mTORC2, IC50=83 nM) complexes of the protein kinase mTOR[4].

In Vivo

PI-103 shows therapeutic activity against a range of human tumor xenografts, exhibiting inhibition of angiogenesis, invasion, and metastasis, as well as direct antiproliferative effects[1]. PI-103 induces immunosuppression promoting in vivo tumor growth and inhibiting apoptosis. Tumors from PI-103-treated mice shows higher levels of cyclin D1 and more proliferating cells[3].

Solvent&Solubility

In Vitro:

DMSO : 25 mg/mL (71.76 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.8706 mL	14.3530 mL	28.7059 mL
5 mM	0.5741 mL	2.8706 mL	5.7412 mL
10 mM	0.2871 mL	1.4353 mL	2.8706 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。

References

[1]. Raynaud FI, et al. Biological properties of potent inhibitors of class I phosphatidylinositide 3-kinases: from PI-103through PI-540, PI-620 to the oral agent GDC-0941. Mol Cancer Ther. 2009 Jul;8(7):1725-39.

[2]. Knight ZA, et al. A pharmacological map of the PI3-K family defines a role for p110 alpha. Cell. 2006 May 19;125(4):733-47.

[3]. Park S, et al. PI-103, a dual inhibitor of Class IA phosphatidylinositide 3-kinase anLeukemia. 2008 Sep;22(9):1698-706.d mTOR, has antileukemicactivity in AmL. Leukemia. 2008 Sep;22(9):1698-706.

[4]. López-Fauqued M, et al. The dual PI3K/mTOR inhibitor PI-103 promotes immunosuppression, in vivo

	tumor growth and increases survival of melanoma cells. Int J Cancer. 2010 Apr 1;126(7):1549-61.
实验参考：	
Cell Assay	For proliferation assays, MOLM14, OCI-AmL3 and MV4-11 cells are cultured during 48 h at 105 cells/mL, in triplicate, in 10% FCS, without or with 0.1 or 1 μM PI-103, and then pulsed 6 h with 1μCi (37 kBq) [4H]-thymidine. The amounts oadioactivity are determined after trichloracetic acid precipitation[2].
Animal Administration	Mice[3] Five to six month old males of either FVB/N strain or nude BALB/c strain are injected subcutaneously with one million cells in PBS. When tumor reaches between 50 and 100 mm^3, mice are treated with 10 mg/kg or 70 mg/kg of PI-103 by IP injection daily. Control mice are treated with the same volume of DMSO. Tumor size and mice weight is monitored every 2 days. When mice are sacrificed, tumors are dissected and processed[3].
Kinase Assay	IC50 values are measured using either a standard thin-layer chromatography (TLC) assay for lipid kinase activity or a high-throughput membrane capture assay. Kinase reactions are performed by preparing a reaction mixture containing kinase, inhibitor (2% DMSO final concentration), buffer (25 mM HEPES, pH 7.4, 10 mM $MgCl_2$), and freshly sonicated phosphatidylinositol (100 μg/mL). Reactions are initiated by the addition of ATP containing 10 μCi of γ-32P-ATP to a final concentration 10 or 100 μM, and allowed to proceed for 20 minutes at room temperature. For TLC analysis, reactions are then terminated by the addition of 105 μL 1N HCl followed by 160 μL CHCl3:MeOH (1:1). The biphasic mixture is vortexed, briefly centrifuged, and the organic phase transferred to a new tube using a gel loading pipette tip precoated with $CHCl_3$. This extract is spotted on TLC plates and developed for 3-4 hours in a 65:35 solution of n-propanol:1M acetic acid. The TLC plates are then dried, exposed to a phosphorimager screen, and quantitated. For each compound, kinase activity is typically measured at 10-12 inhibitor concentrations representing two-fold dilutions from the highest concentration tested (100 μM). For compounds showing significant activity, IC50 determinations are repeated two to four times, and the reported value is the average of these independent measurements[4].
References	[1]. Raynaud FI, et al. Biological properties of potent inhibitors of class I phosphatidylinositide 3-kinases: from PI-103through PI-540, PI-620 to the oral agent GDC-0941. Mol Cancer Ther. 2009 Jul;8(7):1725-39. [2]. Knight ZA, et al. A pharmacological map of the PI3-K family defines a role for p110 alpha. Cell. 2006 May 19;125(4):733-47. [3]. Park S, et al. PI-103, a dual inhibitor of Class IA phosphatidylinositide 3-kinase anLeukemia. 2008 Sep;22(9):1698-706.d mTOR, has antileukemicactivity in AmL. Leukemia. 2008 Sep;22(9):1698-706. [4]. López-Fauqued M, et al. The dual PI3K/mTOR inhibitor PI-103 promotes immunosuppression, in vivo tumor growth and increases survival of melanoma cells. Int J Cancer. 2010 Apr 1;126(7):1549-61.