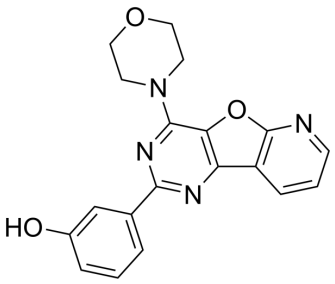
PI-103

Cat. No.:	HY-10115
CAS No.:	371935-74-9
Molecular Formula:	$C_{19}H_{16}N_4O_3$
Molecular Weight:	348.36
Target:	PI3K; mTOR; DNA-PK; Autophagy; Apoptosis
Pathway:	PI3K/Akt/mTOR; Cell Cycle/DNA Damage; Autophagy; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 1 year -20°C 6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 10 mg/mL (28.71 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

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: ≥ 1.05 mg/mL (3.01 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.05 mg/mL (3.01 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PI-103 is a potent PI3K and mTOR inhibitor with IC_{50}s 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. PI-103 induces autophagy[1][2][3][4].

IC_{50} & Target

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

	83 nM (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, IC_{50}=20 nM) and rapamycin-insensitive (mTORC2, IC_{50} =83 nM) complexes of the protein kinase mTOR[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.			
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.			

PROTOCOL

Kinase Assay [4]	IC_{50} 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 $CHCl_3$: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, IC_{50} determinations are repeated two to four times, and the reported value is the average of these independent measurements[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	For proliferation assays, MOLM14, OCI-AmL3 and MV4-11 cells are cultured during 48 h at 10^5 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) [^{4}H]-thymidine. The amounts oadioactivity are determined after trichloracetic acid precipitation[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Adv Funct Mater. 2021 May 24.

- Nat Commun. 2023 Mar 28;14(1):1726.
- Clin Cancer Res. 2020 Apr 15;26(8):2011-2021.
- Clin Cancer Res. 2014 Nov 1;20(21):5483-95.
- Adv Healthc Mater. 2021 Dec 8;e2101944.

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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]. 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.

[3]. 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.

[4]. 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.

Caution: Product has not been fully validated for medical applications. For research use only.

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