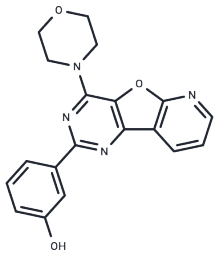
Data Sheet (Cat.No.T6143)

TargetMol

PI-103

Chemical Properties



CAS No. : 371935-74-9

Formula: C19H16N4O3

Molecular Weight: 348.36

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	PI-103 is a potent, cell-permeable, ATP-competitive inhibitor of PI3K family members (IC50s: 2/3/3/15/30/23 nM for p110α/β/δ/γ, mTOR, and DNA-PK).
Targets(IC50)	Apoptosis,Autophagy,DNA-PK,mTOR,PI3K
In vitro	PI-103 potently inhibited p110α (IC50: 15 nmol/L. PI-103 exhibited potent growth inhibition in each of the cell lines examined, with activity in the submicromolar range [1]. PI-103 induced proliferative arrest in a panel of glioma cell lines assayed by flow cytometry. PI-103 uniquely and potently inhibits both complexes of mTOR: the rapamycin-sensitive mTORC1 (IC50: 0.02 μM) and the rapamycin-insensitive mTORC2 (IC50: 0.083 μM). PI-103 (IC50 < 0.1 μM) was blocking the phosphorylation of p70 S6 kinase, ribosomal protein S6, and 4E-BP1, downstream markers of mTOR signaling [2].
In vivo	When tumors reached 50-100 mm^3, animals were randomized and treated with vehicle or PI-103. PI-103 showed significant activity in vivo, reducing average tumor size by 4-fold after 18 days. Preclinical treatment of glioma xenografts with PI-103 blocked proliferation without inducing apoptosis [2]. PI-103 (10 mg/kg) treatment promoted a significant in vivo tumor growth compared with the DMSO treated mice. PI-103 (70 mg/kg) also promoted a significant in vivo tumor growth [3].
Kinase Assay	Phosphatidylinositide 3-kinase inhibitory activity was determined using a scintillation proximity assay in the presence of 1 μmol/L ATP. Inhibition of mTOR protein kinase was determined using a TR-FRET-based LanthaScreen method. Compounds were assayed at a maximum concentration of 10 μmol/L in the presence of 1 μmol/L ATP, and IC50 values were determined using GraphPad Prism software [1].
Cell Research	Human glioma cell lines were obtained from the Brain Tumor Research Center at UCSF. Cells were harvested and fixed, treated with RNAase and propidium iodide, and filtered through 95 mM nylon mesh. Ten thousand stained nuclei were analyzed in a FACS Calibur flow cytometer. DNA histograms were modeled offline using Modifit-LT software. For crystal violet staining, 10^5 cells were seeded in 12-well plates in the presence or absence of PI-103 [2].
Animal Research	Five to six-month-old males of either FVB/N strain or nude BALB/c strain were injected subcutaneously with one million cells in PBS. When the tumor reached between 50 and 100 mm^3, mice were treated with the inhibitors. Treatments were done by IP injection daily with 10 mg/kg or 70 mg/kg of PI-103 and/or 50 mg/kg sorafenib. Control mice were treated with the same volume of DMSO. Tumor size and mice weight was

Animal Research	monitored every 2 days. Tumor volume was calculated with the equation (d^2*D) (p/6). When mice were sacrificed, tumors were dissected and processed. For immunosuppression experiments, mice were treated with rapamycin (1 mg/kg) or LY294002 (25 mg/kg) by a daily IP injection for a total of 8 days [3].

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 10.71 mg/mL (30.74 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+90% Saline: < 1.07 mg/mL (3.07 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. 10% DMSO+90% Corn oil: 1.07 mg/mL (3.07 mM),Solution. 10% DMSO+90% (20% SBE-β-CD in Saline): < 1.07 mg/mL (3.07 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. 10% DMSO+40% PEG300+5% Tween 80+45% Saline: < 1.07 mg/mL (3.07 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.8706 mL	14.353 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
50 mM	0.0574 mL	0.2871 mL	0.5741 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Raynaud FI, et al. Biological properties of potent inhibitors of class I phosphatidylinositide 3-kinases: from PI-103 through PI-540, PI-620 to the oral agent GDC-0941. Mol Cancer Ther. 2009 Jul;8(7):1725-38.

Fan QW, et al. A dual PI3 kinase/mTOR inhibitor reveals emergent efficacy in glioma. Cancer Cell. 2006 May;9(5):341-9.

López-Fauqued M, et al. The dual PI3K/mTOR inhibitor PI-103 promotes immunosuppression, in vivo tumor growth and increases survival of sorafenib-treated melanoma cells. Int J Cancer. 2010 Apr 1;126(7):1549-61.