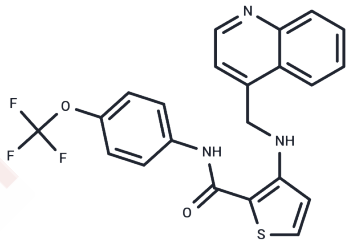
Data Sheet (Cat.No.T2624)

TargetMol

OSI-930

Chemical Properties



CAS No. : 728033-96-3

Formula: C22H16F3N3O2S

Molecular Weight: 443.44

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	OSI-930, an orally active inhibitor of c-Kit and the vascular endothelial growth factor receptor-2 (VEGFR-2), targets cancer cell proliferation and blood vessel growth (angiogenesis) in tumors.
Targets(IC50)	Apoptosis,c-Fms,Raf,FLT,c-Kit,CSF-1R,Src,VEGFR
In vitro	In HMC-1 cell line (IC50=14 nM), OSI-930 inhibited cell proliferation and induced apoptosis.OSI-930 was able to inhibit a variety of recombinant receptor tyrosine kinases, Kit (IC50=80 nM), KDR (IC50=9 nM), Flt (IC50=8 nM), CSF-1R (IC50=15 nM), c- Raf (IC50=41 nM) and Lck (IC50=22 nM).
In vivo	In HMC-1 cell line (IC50=14 nM), OSI-930 inhibited cell proliferation and induced apoptosis.OSI-930 was able to inhibit a variety of recombinant receptor tyrosine kinases, Kit (IC50=80 nM), KDR (IC50=9 nM), Flt (IC50=8 nM), CSF-1R (IC50=15 nM), c- Raf (IC50=41 nM) and Lck (IC50=22 nM).
Kinase Assay	Protein kinase assays : Protein kinase assays are either done in-house by ELISA-based assay methods (Kit, KDR, PDGFRα, and PDGFRβ) or by a radiometric method. In-house ELISA assays used poly(Glu:Tyr) as the substrate bound to the surface of 96-well assay plates; phosphorylation is then detected using an antiphosphotyrosine antibody conjugated to HRP. The bound antibody is then quantitated using ABTS as the peroxidase substrate by measuring the absorbance at 405/490 nm. All assays uses purified recombinant kinase catalytic domains that are either expressed in insect cells or in bacteria. The Kit and EGFR protein used for in-house assays are prepared internally; other enzymes are obtained. Recombinant Kit protein is expressed as an NH2-terminal glutathione S-transferase fusion protein in insect cells and is initially purified as a nonphosphorylated (nonactivated) enzyme with a relatively high Km for ATP (400 μM). In some assays, an activated (tyrosine phosphorylated) form of the enzyme is prepared by incubation with 1 mM ATP for 1 hour at 30 °C. The phosphorylated protein is then passed through a desalting column to remove the majority of the ATP and stored at ?80 °C in buffer containing 50% glycerol. The resultant preparation has a considerably higher specific activity and a lower Km for ATP (25 μM) than the initial nonphosphorylated preparation. The inhibition of Kit autophosphorylation by OSI-930 is assayed by incubation of the nonphosphorylated enzyme at 30 °C in the presence of 200 μM ATP and various concentrations of OSI-930. The reaction is stopped by removal of aliquots into SDS-PAGE sample buffer followed by heating to 100 °C for 5 minutes. The degree of phosphorylation of Kit is then determined by immunoblotting for both total Kit and

	phosphorylated Kit.
Cell Research	For assays of cell proliferation and apoptosis, cells are seeded into 96-well plates and incubated for 2 to 3 days in the presence of OSI-930 at various concentrations. Inhibition of cell growth is determined by luminescent quantitation of the intracellular ATP content using CellTiterGlo. Induction of caspase-dependent apoptosis by OSI-930 is quantitated by an enzymatic caspase 3/7 assay. Inhibition of angiogenesis by OSI-930 is monitored using the rat aortic ring endothelial sprout outgrowth assay. Sections of aorta are prepared from CO2-euthanized male rats and cultured in vitro in a collagen matrix in the presence or absence of OSI-930. The collagen matrix is prepared from type 1 rat tail collagen solubilized in 0.1% acetic acid at 3 mg/mL, which is combined with 0.125 volume collagen buffer (0.05 N NaOH, 200 mM HEPES, 260 mM NaHCO3), 0.125 volume of medium 199, 0.0125 volume of 1 M NaOH, and 1% GlutaMax. Aortic rings are embedded in 0.4 mL of this matrix in six-well plates, to which 0.5 mL endothelial basal medium and the appropriate amount of OSI-930 is added; the rings are then incubated for 10 days and the resultant angiogenic sprout outgrowth is digitally quantitated from images by measurement of the sprout-containing area within a series of concentric rings around the aortic tissue area.(Only for Reference)

Solubility Information

Solubility	DMSO: 82 mg/mL (184.92 mM),Sonication is recommended. Ethanol: 3 mg/mL (6.77 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2551 mL	11.2755 mL	22.551 mL
5 mM	0.451 mL	2.2551 mL	4.5102 mL
10 mM	0.2255 mL	1.1275 mL	2.2551 mL
50 mM	0.0451 mL	0.2255 mL	0.451 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.

Reference

Garton AJ, et al. Cancer Res. 2006, 66(2):1015-1024.
Han H W, Hahn S, Jeong H Y, et al. LINCS L1000 dataset-based repositioning of CGP-60474 as a highly potent anti-endotoxemic agent. Scientific Reports. 2018 Oct 8;8(1):14969
Lin HL, et al. Drug Metab Dispos. 2011, 39(2), 345-350.
Han H W, Hahn S, Jeong H Y, et al. LINCS L1000 dataset-based repositioning of CGP-60474 as a highly potent anti-endotoxemic agent[J]. Scientific reports. 2018 Oct 8;8(1):14969.

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