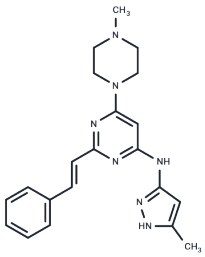
Data Sheet (Cat.No.T2358)

TargetMol

ENMD-2076

Chemical Properties



CAS No. : 934353-76-1

Formula: C21H25N7

Molecular Weight: 375.47

Appearance: no data available

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

Biological Description

Description	ENMD-2076, a multi-targeted kinase inhibitor, has specific activity against Aurora A, Flt3, KDR/VEGFR2, Flt4/VEGFR3, FGFR1, FGFR2, Src, PDGFRα.
Targets(IC50)	Apoptosis,FGFR,FLT,c-RET,Aurora Kinase,PDGFR,Src,VEGFR
In vitro	In the MDA-MB-231 xenograft model, ENMD-2076 was observed to inhibit neovascularization while also inducing regression in already formed vessels. Within the HT29 xenograft model, ENMD-2076 consistently inhibited the activation of Flt3, as well as VEGFR2 / KDR and FGFR1 / 2. In the case of H929 human myeloma xenografts, oral administration of ENMD-2076 (50-200 mg/kg/day) resulted in a significant decrease in phospho-histone 3 (pH3) and Ki-67, alongside a notable increase in cleaved caspase-3, indicating effective antitumor activity through inhibition of cell proliferation and induction of apoptosis.
In vivo	ENMD-2076 targets the PI3K/AKT pathway, leading to the downregulation of apoptosis-inhibiting proteins. It inhibits aurora kinases A and B, causing cell cycle arrest at the G2/M phase. ENMD-2076 is effective against various angiogenesis-related kinases (IC50=1.86-120 nM), including VEGFR2/KDR, VEGFR3, FGFR1, FGFR2, and PDGFRα. In multiple human solid tumor and leukemia cell lines (IC50=0.025-0.7 μM), it induces cell cycle arrest at the G2/M phase and promotes apoptosis.
Kinase Assay	Kinase assays: Recombinant Aurora A and B kinase enzymes and appropriate PanVera Z'-Lyte kinase assay kits are purchased. Assays are carried out in kinase assay buffer (50 mM of HEPES, pH 7.5, 10 mM of MgCl2, 5 mM of EGTA, 0.05% Brij-35) supplemented with 2 mM of DTT. Activities are determined at an ATP concentration equivalent to the apparent Km for each enzyme, and an enzyme concentration that results in approximately 30% phosphorylation of the peptide substrate after 1 hour. Dose-response curves of relative enzyme activity versus ENMD-2076 concentration are plotted with Grafit and used to calculate IC50 values. Potency of ENMD-2076 free base against a select panel of 100 kinase enzymes is determined using the SelectScreen kinase profiling service. ATP concentrations are at the apparent Km for each enzyme or 100 μM if the apparent Km could not be reached. Percent inhibition is determined at an ENMD-2076 free base concentration of 1 μM; for kinases where significant inhibition is noted, IC50 values are determined by generating full 10-point dose-response curves.
Cell Research	The antiproliferative effect of ENMD-2076 on adherent tumor cell lines is measured by plating 500 cells per well in a 96-well plate and incubating with ENMD-2076 for 96

	hours. Cellular proliferation is measured using the sulforhodamine B assay. The leukemia-derived, nonadherent cell lines are assayed by plating 5 × 103 cells per well in a 96-well plate. The cells are incubated with ENMD-2076 for 48 hours and then survival is assayed using the Alamar Blue reagent. To measure the effect of ENMD-2076 on VEGF- and fibroblast growth factor (FGF)-induced proliferation of human umbilical vein endothelial cell (HUVEC), cells are serum starved for 6 hours, then treated with ENMD-2076 free base, and stimulated with 5 ng/mL bFGF or 25 ng/mL VEGF (R and D Systems) for 72 hours. Cell proliferation is measured using WST-(Only for Reference)

Solubility Information

Solubility	DMSO: 97 mg/mL (258.34 mM),Sonication is recommended. H2O: 1 mg/mL (2.66 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.6633 mL	13.3166 mL	26.6333 mL
5 mM	0.5327 mL	2.6633 mL	5.3267 mL
10 mM	0.2663 mL	1.3317 mL	2.6633 mL
50 mM	0.0533 mL	0.2663 mL	0.5327 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

Fletcher GC, et al, Mol Cancer Ther, 2011, 10(1), 126-137.
Wang X, et al. Br J Haematol, 2010, 150(3), 313-325.