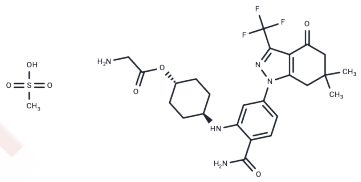
Data Sheet (Cat.No.T4342)

TargetMol

PF-04929113 Mesylate

Chemical Properties



CAS No. : 1173111-67-5

Formula: C26H34F3N5O7S

Molecular Weight: 617.63

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	PF-04929113 Mesylate (SNX-5422 Mesylate), a prodrug of SNX-2112, is an orally available Hsp90 inhibitor (Kd: 41 nM) and also induces Her-2 degradation (IC50: 37 nM).
Targets(IC50)	HSP,HER
In vitro	PF-04929113 effectively inhibits Her2 (IC50: 5?±?1 nM) and p-ERK stability in AU565 cells (IC50: 11?±?3 nM) and p-S6 (IC50: 61?±?22 nM) in A375 cells. PF-04929113 also induces Hsp70 in A375 cells (IC50: 13?±?3 nM). PF-04929113 (0.5, 1, 2, 5, and 10 μM) concentration-dependently reduces cell viability. Furthermore, PF-04929113 (1, 3, 5, 7 μM) in combination with equal amounts of HDAC inhibitors (PXD101, SAHA, and TSA) synergistically induces cell death via suppression of PI3K/Akt/mTOR signaling in ATC cells.
In vivo	In HT-29 human colon tumor xenograft model, PF-04929113 (50 mg/kg, p.o.) potently inhibits tumor growth after administration 3 times a week for 3 weeks (qod × 3/2 × 3). PF-04929113 (20/40 mg/kg, p.o.) markedly inhibits multiple myeloma (MM) tumor angiogenesis and growth in mice.
Kinase Assay	Briefly, Hsp90 from porcine spleen extract is isolated by affinity capture on a purine-affinity media. The Hsp90 loaded media is then challenged with test compound (PF-04929113) at a given concentration, ranging from 0.8 to 500 μM, and the amount of Hsp90 liberated at each concentration is determined. The resulting IC50 values are corrected for the ATP ligand concentration and presented as apparent Kd values.
Cell Research	PF-04929113 is dissolved in DMSO.Cell viability is determined by the CCK-8 Assay Kit. Cells (5 × 103/100 μL) in each well on 96-well plates are incubated overnight and treated with the drugs (PF-04929113) for an additional 4 h at 37°C. Absorbance is measured at 450 nm using a spectrophotometer.
Animal Research	PF-04929113 is preformulated in 1% microcrystalline cellulose/0.5% Tween80 in water. Female nude mice are 11 to 12 weeks old and have a body weight range of 18.7?30.5 g on Day 1 of the study. Xenografts are initiated from HT-29 human colon carcinoma tumors maintained by serial transplantation in athymic nude mice. Each test mouse receives a 1 mm3 HT-29 tumor fragment implanted subcutaneously in the right flank, and the growth of tumors is monitored as the average size approached 80?120 mm3. Fourteen days later, designated as Day 1 of the study, individual tumor volumes range from 63 to 126 mm3 and the animals are placed into eight groups, each consisting of 10 mice with group mean tumor volumes of 93.2?93.9 mm3. Micronized PF-04929113 is

Animal Research	preformulated in 1% microcrystalline cellulose/0.5% Tween80 in water. The solutions are stored at 4°C during the study and homogenized just prior to dosing. Group 1 vehicle control mice receive D5W (5% dextrose) vehicle by oral gavage beginning on Day 1, every other day for three doses, followed by two days without treatment, for three cycles ((qod × 3)/2 × 3 weeks, a total of nine doses). Groups 2 to 5 animals receive 10 at 5, 10, 25, or 50 mg/kg on the same schedule as vehicle control group ((qod × 3)/2 × 3). Each treatment is administered in a volume of 0.2 mL per 20 g of body weight (10 mL/kg) and is scaled to the body weight of the animal. Tumors are measured twice weekly using calipers.

Solubility Information

Solubility	DMSO: 27.5 mg/mL (44.53 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.6191 mL	8.0955 mL	16.1909 mL
5 mM	0.3238 mL	1.6191 mL	3.2382 mL
10 mM	0.1619 mL	0.8095 mL	1.6191 mL
50 mM	0.0324 mL	0.1619 mL	0.3238 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

Huang KH, et al. Discovery of novel 2-aminobenzamide inhibitors of heat shock protein 90 as potent, selective and orally active antitumor agents. J Med Chem. 2009 Jul 23;52(14):4288-305
Chandarlapaty S, et al. SNX2112, a synthetic heat shock protein 90 inhibitor, has potent antitumor activity against HER kinase-dependent cancers. Clin Cancer Res. 2008 Jan 1;14(1):240-8.
Kim SH, et al. The heat shock protein 90 inhibitor SNX5422 has a synergistic activity with histone deacetylase inhibitors in induction of death of anaplastic thyroid carcinoma cells. Endocrine. 2016 Feb;51(2):274-82.
Okawa Y,etal.SNX-2112, a selective Hsp90 inhibitor, potently inhibits tumor cell growth, angiogenesis, and osteoclastogenesis in multiple myeloma and other hematologic tumors by abrogating signaling via Akt and ERK. Blood. 2009 Jan 22;113(4):846-55.

Tel:781-999-4286 E_mail:info@targetmol.com Address:34 Washington Street,Wellesley Hills,MA 02481