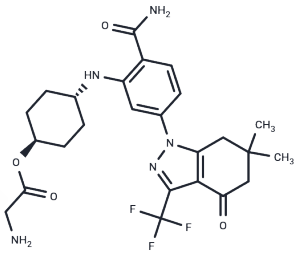
Data Sheet (Cat.No.T6341)

TargetMol

PF04929113

Chemical Properties



CAS No. : 908115-27-5

Formula: C25H30F3N5O4

Molecular Weight: 521.53

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	PF04929113 (SNX-5422) is a synthetic, novel, small molecule Hsp90 Inhibitor. As an oral formulation that demonstrates strong efficacy and tolerability, PF04929113 is positioned as a breakthrough therapy with broad applicability across a wide range of cancers.
Targets(IC50)	HSP,HER
In vitro	PF-04929113 showed potent effects on Her-2 stability and led to the expected upregulation of Hsp70.PF-04929113 showed potent antiproliferative activity against a wide range of cancer cell types, e.g., MCF-7 (IC50 = 16 nM), SW620 (IC50 = 19 nM), K562 (IC50 = 23 nM), SK- MEL-5 (IC50 = 25 nM) and A375 (IC50 = 51 nM).
In vivo	PF-04929113 showed potent effects on Her-2 stability and led to the expected upregulation of Hsp70.PF-04929113 showed potent antiproliferative activity against a wide range of cancer cell types, e.g., MCF-7 (IC50 = 16 nM), SW620 (IC50 = 19 nM), K562 (IC50 = 23 nM), SK- MEL-5 (IC50 = 25 nM) and A375 (IC50 = 51 nM).
Kinase Assay	The Hsp90 loaded media is challenged with PF-04929113 at a given concentration, ranging from 0.8 to 500 μM, and the amount of Hsp90 liberated at each concentration is determined by Bradford protein assay. The resulting IC50 values are corrected for the ATP ligand concentration and presented as apparent Kd values.
Cell Research	Cell lines: MCF-7,SW620,K562,SK-MEL-5 and A375 cancer cell lines. Concentrations: 0-300 nM. Method: Proliferation rates are measured by seeding cells into 96-well plates, followed by compound addition 24 h later.After addition of PF-04929113,cells are allowed to grow for either an additional 72 or 144 h depending on the rate of growth.At harvest,media is removed and DNA content for individual wells is determined using CyQuant DNA dye.Levels of Hsp90 client proteins and phosphor-regulated proteins in A375 are measured by high content analysis (HCA) using an ArrayScan 4.5 instrument after 24 hours of treatment with PF-04929113,followed by methanol fixation.After fixation in 4% PBS-buffered formalin and permeablization with 0.1% TX-100,cells are probed with anti-Her2,antiphospho-S6 (pS6),antipERK,and anti-Hsp70 primary antibodies,followed by TRITC or FITC conjugated secondary antibodies.Nuclei are also stained with Hoechst DNA binding dye.For each well,250-500 individual nuclei are identified along with the average staining intensity for the client and phospho-proteins for each cell.Average client staining intensities are then calculated for each well.
Animal Research	Animal Models: 5 ×106 MM.1S cells are inoculated subcutaneously in the Fox Chase SCID mice (6-7 weeks old). Formulation: PF-04929113 is dissolved in 1% carboxy methylcellulose/0.5% Tween 80 at 10 mg/mL and stored at 4 °C. Dosages: 20 or 40

Animal Research	mg/kg. Administration: orally 3 times per week,3 weeks in total.

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: 3 mg/mL (5.75 mM),Sonication is recommended. DMSO: 120 mg/mL (230.09 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 10 mg/mL (19.17 mM),Solution. 10% DMSO+90% Saline: < 10 mg/mL (19.17 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	1.9174 mL	9.5872 mL	19.1744 mL
5 mM	0.3835 mL	1.9174 mL	3.8349 mL
10 mM	0.1917 mL	0.9587 mL	1.9174 mL
50 mM	0.0383 mL	0.1917 mL	0.3835 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, J Med Chem, 2009, 52(14), 4288-4305
Yutaka Okawa, et al, Blood, 2009, 113(4), 846-855.
Lamoureux F, et al, Clin Cancer Res, 2011, 17(8), 2301-2313.