Product Data Sheet

Product Name: PF-04929113 (SNX-5422)
Cat. No.: GC11912

Chemical Properties

Cas. No.	908115-27-5		
Chemical Name	[4-[2-carbamoyl-5-[6,6-dimethyl-4-oxo-3-(trifluoromethyl)-5,7-dihydroindazol-1-yl]anilino]cyclohexyl] 2-aminoacetate		
SMILES	CC1(CC2=C(C(=O)C1)C(=NN2C3=CC(=C(C=C3)C(=O)N)NC4CCC(CC4)OC(=O)CN)C(F)(F)F)C		
Formula	$C_{25}H_{30}F_3N_5O_4$	M.Wt	521.5
Solubility	≥ 23.85 mg/mL in DMSO with gentle warming	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	PF-04929113 (SNX-5422)		

Protocol

Kinase experiment [1]:

Affinity for Hsp90	Hsp90 from porcine spleen extract was isolated by affinity capture on a purine-affinity media. The Hsp90 loaded media was then challenged with PF-04929113 at a given concentration, ranging from 0.8 to 500 μM, and the amount of Hsp90 liberated at each concentration was determined by Bradford protein assay. The resulting IC50 values were corrected for the ATP ligand concentration and presented as apparent Kd values.

Cell experiment [1]:

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Cell lines	MCF-7, SW620, K562, SK-MEL-5 and A375 cancer cell lines
Preparation method	The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.
Reaction Conditions	0 ~ 300 nM; 72 or 144 hrs
Applications	In a broad range of cancer cell lines (MCF-7, SW620, K562, SK-MEL-5 and A375 cells), PF-04929113 showed potent antiproliferative activity, with the IC50 values being 16, 19, 23, 25 and 51 nM, respectively.

Animal experiment [2]:

Animal models	Fox Chase SCID mice (6 ~ 7 weeks old) inoculated subcutaneously with 5 × 106 MM.1S cells
Dosage form	20 or 40 mg/kg; p.o.; 3 times per week, for 3 weeks
Applications	PF-04929113 inhibited human MM cell growth and angiogenesis in vivo.

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Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

[1]. Huang KH, Veal JM, Fadden RP, Rice JW, Eaves J, Strachan JP, Barabasz AF, Foley BE, Barta TE, Ma W, Silinski MA, Hu M, Partridge JM, Scott A, DuBois LG, Freed T, Steed PM, Ommen AJ, Smith ED, Hughes PF, Woodward AR, Hanson GJ, McCall WS, Markworth CJ, Hinkley L, Jenks M, Geng L, Lewis M, Otto J, Pronk B, Verleysen K, Hall SE. 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.

[2]. Okawa Y, Hideshima T, Steed P, Vallet S, Hall S, Huang K, Rice J, Barabasz A, Foley B, Ikeda H, Raje N, Kiziltepe T, Yasui H, Enatsu S, Anderson KC. 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.

Background

PF-04929113 is an inhibitor of Hsp90 [1].

PF-04929113 is a water-soluble and oral pre-PF-04928473, which can be rapidly absorbed and converted into PF-04928473 after oral administration. In BT-474 xenograft mice, PF-04928473 induced the degradation of HER2 client protein. No obvious toxicity was observed when the dose reached 150mg/kg. PF-04928473 at 100mg/kg resulted in complete tumor growth inhibition and

local tumor regression in some mice. In H1650 xenograft mice, PF-04928473 also showed significant anti-tumor activity. In addition, as an inhibitor of Hsp90, PF-04928473 inhibits p-ERK and p-Akt in vivo, reduces CD31+ cells and MVD, and has an effect on angiogenesis [1,2].

References:

[1] Chandarlapaty S, Sawai A, Ye Q, Scott A, Silinski M, Huang K, Fadden P, Partdrige J, Hall S, Steed P, Norton L, Rosen N, Solit DB. 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.

[2] Okawa Y, Hideshima T, Steed P, Vallet S, Hall S, Huang K, Rice J, Barabasz A, Foley B, Ikeda H, Raje N, Kiziltepe T, Yasui H, Enatsu S, Anderson KC. 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.

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