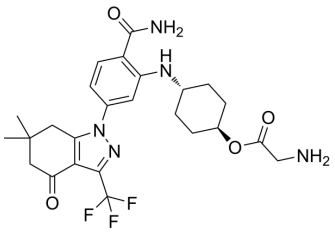
SNX-5422

Cat. No.:	HY-10213
CAS No.:	908115-27-5
Molecular Formula:	$C_{25}H_{30}F_3N_5O_4$
Molecular Weight:	521.53
Target:	HSP
Pathway:	Cell Cycle/DNA Damage; Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 32.5 mg/mL (62.32 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 3.25 mg/mL (6.23 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 3.25 mg/mL (6.23 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SNX-5422 (PF-04929113), a prodrug of SNX-2112, is an orally active Hsp90 inhibitor, with a K_d of 41 nM, and also induces Her-2 degradation, with an IC_{50} of 37 nM.

IC_{50} & Target

IC50: 37 nM (Her-2)[1]
Kd: 41 nM (Hsp90)[1]

In Vitro

SNX-5422 is an orally active Hsp90 inhibitor, with a K_d of 41 nM, and also induces Her-2 degradation, with an IC_{50} of 37 nM. SNX-5422 exhibits potent effects on Her2 and p-ERK stability in AU565 cells and p-S6 in A375 cells, with IC_{50}s of 5 ± 1, 11 ± 3, and 61 ± 22 nM, respectively. SNX-5422 also induces Hsp70 in A375 cells with an IC_{50} of 13 ± 3 nM[1]. SNX-5422 (SNX5422; 0.5, 1, 2, 5, and 10 μM) reduces cell viability in a concentration-dependent manner. Moreover, SNX-5422 (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[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	SNX-5422 (50 mg/kg, p.o.) efficiently inhibits tumor growth of HT-29 human colon tumor xenograft model after administration 3 times a week for 3 weeks (qod×3/2×3)[1]. SNX-5422 (20, 40 mg/kg, p.o.) markedly inhibits multiple myeloma (MM) tumor growth and angiogenesis in mice[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	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 (SNX-5422) at a given concentration, ranging from 0.8 to 500 μM, and the amount of Hsp90 liberated at each concentration is determined. The resulting IC_{50} values are corrected for the ATP ligand concentration and presented as apparent K_d values[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [3]	Cell viability is determined by the CCK-8 Assay Kit. Cells (5×10^3/100 μL) in each well on 96-well plates are incubated overnight, and treated with the drugs (SNX-5422) for an additional 4 h at 37°C. Absorbance is measured at 450 nm using a spectrophotometer. All experiments are performed in triplicate[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	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 mm^3 HT-29 tumor fragment implanted subcutaneously in the right flank, and the growth of tumors is monitored as the average size approached 80–120 mm^3. Fourteen days later, designated as Day 1 of the study, individual tumor volumes range from 63 to 126 mm^3 and the animals are placed into eight groups, each consisting of 10 mice with group mean tumor volumes of 93.2–93.9 mm^3. Micronized SNX-5422 is 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, 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[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. 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

[2]. 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.

[3]. 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.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA