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Produktinformation

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Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

Zuschläge

- Mindermengenzuschlag
- Trockeneiszuschlag
- Gefahrgutzuschlag
- Expressversand

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SNX-2112

Cat. No.: HY-10214

CAS No.: 908112-43-6

Molecular Formula: $C_{23}H_{27}F_3N_4O_3$

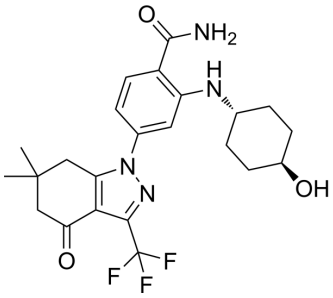
Molecular Weight: 464.48

Target: HSP; Autophagy

Pathway: Cell Cycle/DNA Damage; Metabolic Enzyme/Protease; Autophagy

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 : 25 mg/mL (53.82 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1529 mL	10.7647 mL	21.5295 mL
5 mM	0.4306 mL	2.1529 mL	4.3059 mL
10 mM	0.2153 mL	1.0765 mL	2.1529 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: ≥ 2.5 mg/mL (5.38 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.38 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.38 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SNX-2112 (PF 04928473) is an orally active Hsp90 inhibitor, with a K_d of 16 nM for Hsp90 and IC_{50}s of 30 nM, 30 nM for Hsp90 α and Hsp90 β, also induces Her-2 degradation, and inhibits Grp94 and Trap-1, with IC_{50}s of 10 nM, 4.275 μM and 0.862 μM, respectively[1]. SNX-2112 (PF 04928473) binds Hsp90 isoforms Hsp90α, Hsp90β and Hsp90b1/Grp94 with K_ds of 4 nM, 6 nM and 484 nM, respectively[2].

IC_{50} & Target	HSP90α	HSP90β	GRP94	TRAP-1
	30 nM (IC_{50})	30 nM (IC_{50})	4275 nM (IC_{50})	862 nM (IC_{50})

In Vitro

SNX-2112 is an orally active Hsp90 inhibitor, with a K_d of 16 nM, and also induces Her-2 degradation, with an IC_{50} of 10 nM[3]. SNX-2112 binds to Hsp90, with IC_{50}s of 30 nM, 30 nM, 4.275 μM and 0.862 μM for Hsp90 α and β, Grp94 and Trap-1, respectively[1]. SNX-2112 shows potent antiproliferative activity against various cancer cell types, with IC_{50}s of 3 nM to 53 nM. SNX-2112 exhibits potent effects on Her2 and p-ERK stability in AU565 cells and p-S6 in A375 cells, with IC_{50}s of 11 ± 5, 41 ± 12, and 1 ± 0.6 nM, respectively. SNX-2112 also induces Hsp70 in A375 cells with an IC_{50} of 2 ± 0.9 nM[3]. In addition, SNX-2112 potently blocks signaling of Hsp90 clients, such as Akt, ERK, and NF-κB pathways in different cells. SNX-2112 inhibits multiple myeloma (MM) cell growth, including MM.1S, U266, INA-6, RPMI8226, OPM1, OPM2, MM.1R, and Dox40 MM cell lines, with IC_{50}s of 52, 55, 19, 186, 89, 67, 93, and 53 nM at 48 hours, respectively. SNX-2112 (2.5-10 nM) also suppresses osteoclast formation, associated with down-regulation of ERK/c-fos and PU.1[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [4]

To measure proliferation of multiple myeloma (MM) cells and bone marrow stromal cells (BMSCs), the rate of DNA synthesis is measured. MM cells are incubated in 96-well culture plates in the presence of SNX-2112 and/or IL-6 or IGF-1 or BMSCs for 48 hours. Cells are pulsed with 0.5 μCi/well of [^{3}H]-thymidine during the last 8 hours of culture, harvested onto glass filters with an automatic cell harvester, and counted using the LKB Betaplate scintillation counter. Inhibition of proliferation by test compounds (SNX-2112) in solid tumor cell lines is measured in 96-well plates after 72 hours of treatment with Cyquant DNA binding dye. AML, LCL, and K562 cell line proliferation rates are measured after 72 hours of compound treatment with CellTiter-Glo[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Theranostics. 2019 Aug 12;9(20):5769-5783.
- J Pharm Biomed Anal. 2017 Sep 5;143:94-100.

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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]. Okawa Y, et al. 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.

[4]. Mishra SJ, et al. Transformation of the Non-Selective Aminocyclohexanol-Based Hsp90 Inhibitor into a Grp94-Seletive Scaffold. ACS Chem Biol. 2017 Jan 20;12(1):244-253.

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