
Product Data Sheet

Product Name: SNX-2112

Cat. No.: GC13946

Chemical Properties

Cas. No. 908112-43-6

Chemical Name 4-[6,6-dimethyl-4-oxo-3-(trifluoromethyl)-5,7-dihydroindazol-1-yl]-2-[(4-hydroxycyclohexyl)amino]benzamide

SMILES CC1(CC2=C(C(=O)C1)C(=NN2C3=CC(=C(C=C3)C(=O)N)NC4CCC(CC4)O)C(F)(F)F)CFormula C₂₃H₂₇F₃N₄O₃ M.Wt 464.48

Solubility ≥ 23.05 mg/mL in DMSO, ≥ 9.6 mg/mL in EtOH with ultrasonic and warming Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C 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 **Protocol****Cell experiment [1]:**

Cell lines HepG2 cells

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Preparation Method HepG2 cells were cultured in DMEM medium containing 10% FBS (fetal bovine serum) and 100U/ml penicillin-streptomycin and incubated at 37°C in the presence of 5% CO₂. Cells were seeded in 96-well plates at a density of 5×10⁴ cells/ml, 100µl medium was added to each well, and cultured overnight. The cells were treated with different concentrations of SNX-2112 (0.01, 0.1, 1, and 10µM) for 72 hours and then analyzed for cell viability.

Reaction Conditions 0.01, 0.1, 1, and 10µM; 72h

Applications SNX-2112 treatment reduced the cell viability of HepG2 cells in a dose-dependent manner.

Animal experiment [2]:

Animal models NOD/SCID mice

Preparation Method 6-week-old NOD/SCID mice were housed in a specific pathogen-free (SPF) animal house maintained at 23°C with a 12h light/dark cycle and free access to water and food. Eight mice per group were inoculated via the tail vein with 1×10⁷ K562 cells. SNX-2112 at a dose of 6mg/kg was injected via the tail vein starting on the fifth day of K562 cell implantation, 5 times a week for 2 weeks, and the expression levels of CD13⁺ and CD33⁺ were measured.

Dosage form 6mg/kg; 5 times a week for 2 weeks; tail vein injection

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Applications SNX-2112 treatment significantly inhibited the expression levels of CD13⁺ and CD33⁺ in NOD/SCID mice inoculated with K562 cells.

References:

[1] Wang X, Wang S, Liu Y, et al. The Hsp90 inhibitor SNX-2112 induces apoptosis of human hepatocellular carcinoma cells: the role of ER stress[J]. Biochemical and biophysical research communications, 2014, 446(1): 160-166.

[2] Jin L, Xiao C L, Lu C H, et al. Transcriptomic and proteomic approach to studying SNX-2112-induced K562 cells apoptosis and anti-leukemia activity in K562-NOD/SCID mice[J]. FEBS letters, 2009, 583(12): 1859-1866.

Background

SNX-2112 is a potent inhibitor of synthetic heat shock protein (Hsp 90) with an IC₅₀ value of 30nM^[1]. SNX-2112 inhibits tube formation by human umbilical vein endothelial cells via abrogation of the eNOS/Akt pathway and markedly inhibits osteoclast formation via down-regulation of ERK/c-fos and PU.1^[2]. SNX-2112 has been widely used to inhibit tumor progression as well as to induce degradation of HSP-90 substrate proteins in cellular and animal models^[3].

In vitro, SNX-2112 treatment for 72 hours significantly inhibited the viability of HepG2,

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Huh7, and SK-Hep1 cells, with IC₅₀ values of 0.36μM, 0.12μM and 0.24μM, respectively^[4]. Treatment with 125nM SNX-2112 for 48 hours inhibited Akt/mTOR signaling pathway, upregulated LC3-II and Beclin1 expression, and induced autophagy in HeLa cells^[5]. Treatment with SNX-2112 at 0.2μM for 48h significantly induced apoptosis in A-375 cells, accompanied by chromatin condensation, marginalization, and DNA fragmentation^[6].

In vivo, SNX-2112 treatment via oral administration at a daily dose of 80mg/kg for 15 days significantly inhibited tumor growth in a B16 cell xenograft tumor mouse model and resulted in a reduction in intratumoral vessel density^[7]. Intravenous injection of 6mg/kg SNX-2112 (five times a week) for two consecutive weeks significantly inhibited the expression levels of CD13⁺ and CD33⁺ in NOD/SCID mice inoculated with K562 cells and prolonged the survival time of the mice^[8].

References:

- [1] Chandarlapaty S, Sawai A, Ye Q, et al. SNX2112, a synthetic heat shock protein 90 inhibitor, has potent antitumor activity against HER kinase-dependent cancers[J]. *Clinical Cancer Research*, 2008, 14(1): 240-248.
- [2] Okawa Y, Hideshima T, Steed P, 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[J]. *Blood, The Journal of the American Society of Hematology*, 2009, 113(4): 846-855.
- [3] Bachleitner-Hofmann T, Sun M Y, Chen C T, et al. Antitumor activity of SNX-2112, a synthetic heat shock protein-90 inhibitor, in MET-amplified tumor cells with or without resistance to selective MET Inhibition[J]. *Clinical Cancer Research*, 2011, 17(1): 122-133.
- [4] Wang X, Wang S, Liu Y, et al. The Hsp90 inhibitor SNX-2112 induces apoptosis of human hepatocellular carcinoma cells: the role of ER stress[J]. *Biochemical and biophysical research communications*, 2014, 446(1): 160-166.
- [5] Hu L, Wang Y, Chen Z, et al. Hsp90 inhibitor SNX-2112 enhances TRAIL-Induced apoptosis of human cervical cancer cells via the ROS-mediated JNK-p53-autophagy-DR5 pathway[J]. *Oxidative medicine and cellular longevity*, 2019, 2019(1): 9675450.
- [6] Liu K S, Liu H, Qi J H, et al. SNX-2112, an Hsp90 inhibitor, induces apoptosis and autophagy via degradation of Hsp90 client proteins in human melanoma A-375 cells[J]. *Cancer letters*, 2012, 318(2): 180-188.

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- [7] Liu K S, Ding W C, Wang S X, et al. The heat shock protein 90 inhibitor SNX-2112 inhibits B16 melanoma cell growth in vitro and in vivo[J]. *Oncology reports*, 2012, 27(6): 1904-1910.
- [8] Jin L, Xiao C L, Lu C H, et al. Transcriptomic and proteomic approach to studying SNX-2112-induced K562 cells apoptosis and anti-leukemia activity in K562-NOD/SCID mice[J]. *FEBS letters*, 2009, 583(12): 1859-1866.

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