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Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

Zuschläge

- Mindermengenzuschlag
- Trockeneiszuschlag
- Gefahrgutzuschlag
- Expressversand

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Zelavespib

Cat. No.: HY-11038

CAS No.: 873436-91-0

Molecular Formula: $C_{18}H_{21}IN_6O_2S$

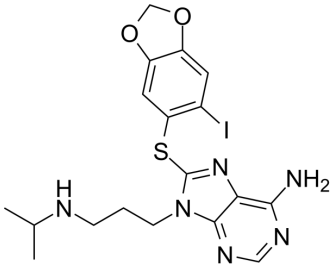
Molecular Weight: 512.37

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 : ≥ 100 mg/mL (195.17 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9517 mL	9.7586 mL	19.5171 mL
	5 mM	0.3903 mL	1.9517 mL	3.9034 mL
	10 mM	0.1952 mL	0.9759 mL	1.9517 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 (4.88 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.88 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.88 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Zelavespib (PU-H71) is a potent Hsp90 inhibitor, with an IC_{50} of 51 nM in MDA-MB-468 cells.

IC_{50} & Target

HSP90

51 nM (IC_{50}, MDA-MB-468 cells)

In Vitro

Zelavespib is a potent Hsp90 inhibitor, with an IC_{50} of 51 nM in MDA-MB-468 cells. Zelavespib inhibits the growth of several

tumor cells, such as MDA-MB-468, MDA-MB-231 and HCC-1806 cells, with IC_{50}s of 65 ± 8 nM, 140 ± 5 nM and 87 ± 3 nM, respectively, and such inhibition is associated with a G2-M block arrest. Zelavespib (10-1000 nM) induces significant apoptosis in triple-negative breast cancers (TNBCs). Zelavespib (0.5, 1 μM) also downregulates oncoproteins involved in the invasive potential of TNBCs[1]. Zelavespib (0.5 μM) decreases and depletes the BCR signaling kinases. Zelavespib (0.25-10 μM) is cytotoxic to CLL cells but shows minimal effects on PBMC or resting B cells. In addition, Zelavespib (0-1 μM) reduces CLL viability via the induction of mitochondrial apoptosis, and antagonizes the survival signals from CLL microenvironment at 0.5 μM[2]. Zelavespib (0.05 μM) induces apoptosis of MDA-MB-231, BT-474, and MCF7 cells, and such induction is enhanced by TNF-α. Zelavespib (0.05 μM) degradates IKKβ, and down-regulates the NF-κB transcriptional activity induced by TNF-α treatment[3].

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

In Vivo

Zelavespib (75 mg/kg, i.p.) causes intratumor accumulation, extends down-regulation of anti-tumor driving molecules, completes and retains responses at nontoxic doses in MDA-MB-468 tumor-bearing mice. Zelavespib(75 mg/kg 3×week, i.p.) suppresses the gowth of tumors, and such an effect is associated with down-regulation of several Hsp90-regulated malignancy driving proteins[1].

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

PROTOCOL

Kinase Assay [1]

Measurements are performed in black 96-well microtiter plates. In short, cell lysates are prepared by rupturing cellular membranes by freezing at -70°C and dissolving the cellular extract in HFB [20 mM Hepes (K), pH 7.3, 50 mM KCl, 5 mM $MgCl_2$, 20 mM Na_2MoO_4, 0.01% Nonidet P-40] with added protease and phosphatase inhibitors (Zelavespib, etc.). Saturation curves are recorded in which fluorescently labeled geldanamycin (Cy3B-GM) (3 nM) is treated with increasing amounts of cellular lysates. The amount of lysate that results in polarization (mP) readings corresponding to 90%-99% bound ligand is chosen for the competition study. Here, each 96-well plate contains 3 nM Cy3B-GM, cellular lysate and tested Hsp90 inhibitor in a final volume of 100 μL. The plate is left for 24 h on a shaker at 4°C, and the fluorescence polarization (FP) values in mP are recorded. EC_{50} values are determined as the competitor concentrations at which 50% of the Cy3B-GM is displaced. FP measurements are performed on an Analyst GT microplate reader[1].

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

Cell Assay [1]

The antiproliferative effects of select Hsp90 inhibitors is evaluated using the CellTiter-Glo Luminescent Cell Viability Assay kit. Briefly, exponentially growing MDA-MB-468, MDA-MB-231, and HCC-1806 cells are seeded into black 96-well microtiter plates and incubated in medium containing either vehicle control (DMSO) or Zelavespib for the indicated time at 37°C. Plates containing 3 replicate wells per assay condition are seeded at a density of 8×10^3 cells for each cell line in 100 μL medium. After exposure of cells to the Hsp90 inhibitors, plates are equilibrated to room temperature (20-25°C) for approximately 30 min, and 100 μL CellTiter-Glo reagent are added to each well. Plates are mixed for 2 min on an orbital shaker and then incubated for 15 min to 2 h at room temperature. The luminescence signal in each well is measured in an Analyst GT microplate reader. The percentage cell growth inhibition is calculated by comparing luminescence readings obtained from treated versus control cells, accounting for initial cell population (time 0). The IC_{50} is calculated as the drug concentration that inhibits cell growth by 50%[1].

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Animal Administration [1]

Mice[1]

Mice bearing MDA-MB-468 tumors reaching a volume of 100-150 mm^3 are treated i.p. using different doses and schedules: Group 01 (n = 8) PBS; group 02 (n = 8) Zelavespib at 50 mg/kg on alternate days; group 03 (n = 8) Zelavespib at 50 mg/kg 5xqd ; group 04 (n = 8) Zelavespib at 75 mg/kg 3 week; group 05 (n = 8) Zelavespib at 75 mg/kg on alternate days. Mice bearing HCC-1806 or MDA-MB-231 xenografted tumors receive Zelavespib at 75 mg/kg on alternate days. Tumor volume is determined by measurement with Vernier calipers, and tumor volume is calculated as the product of its length × $width^2$ × 0.4. Tumor volume is expressed on indicated days as the median tumor volume ± SD indicated for groups of mice[1].

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

REFERENCES

[1]. Caldas-Lopes E, et al. Hsp90 inhibitor PU-H71, a multimodal inhibitor of malignancy, induces complete responses in triple-negative breast cancer models. Proc Natl Acad Sci U S A. 2009 May 19;106(20):8368-73.

[2]. Guo A, et al. HSP90 stabilizes B-cell receptor kinases in a multi-client interactome: PU-H71 induces CLL apoptosis in a cytoprotective microenvironment. Oncogene. 2017 Jun 15;36(24):3441-3449.

[3]. Qu Z, et al. PU-H71 effectively induces degradation of IκB kinase β in the presence of TNF-α. Mol Cell Biochem. 2014 Jan;386(1-2):135-42.

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