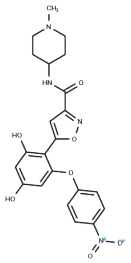
Data Sheet (Cat.No.T6609)

TargetMol

NMS-E973

Chemical Properties



CAS No. : 1253584-84-7

Formula: C22H22N4O7

Molecular Weight: 454.43

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	NMS-E973 is a potent and selective Hsp90 inhibitor with a DC50 of less than 10 nM for Hsp90 binding, displaying no activity against a panel of 52 diverse protein kinases.
Targets(IC50)	HSP
In vitro	NMS-E973 shows a widespread antiproliferative activity with an average IC50 of 1.6 μM, and induces the degradation of client protein, such as Flt3, B-Raf, AKT, which further blocks tumor-related pathways, such as the Raf/MAPK, PI3K/AKT, and JAK/STAT pathways. [1]
In vivo	NMS-E973 (10 mg/kg i.v.) shows a favorable pharmacokinetic profile with selective retention in tumor tissue and ability to cross the BBB. NMS-E973 (60 mg/kg i.v.) shows high antitumor efficacy in all the models tested, including A375 and A2780 xenografts. In addition, NMS-E973 (10 mg/kg i.v.) together with B-Raf inhibitor PLX-4720 at 100 mg/kg produces a synergic anti-tumor effect. [1] In a mouse model of human ovarian cancer, NMS-E973 produces the antitumor activity by inhibition of Hsp90. [2]
Kinase Assay	Hsp90 binding assays: For competition experiments, a protein concentration of 5 nM for Hsp90 and of 200 nM for Trap1 are mixed with 0.5 nmol/L probe (final concentrations). After incubation, the dimethyl sulfoxide (DMSO) compound solution is added to the mixture. The plate is incubated for 18 hours at room temperature and then the fluorescence polarization signal was measured. Data are fitted with the program Dynafit version 3.28.039 or SigmaPlot (SSI) using the mathematical equation for competitive binding of 2 ligands to the receptor.

Solubility Information

Solubility	DMSO: 83 mg/mL (182.65 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 3.3 mg/mL (7.26 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may*

In vivo Formulation	*vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2006 mL	11.0028 mL	22.0056 mL
5 mM	0.4401 mL	2.2006 mL	4.4011 mL
10 mM	0.2201 mL	1.1003 mL	2.2006 mL
50 mM	0.044 mL	0.2201 mL	0.4401 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Fogliatto G, et al. Clin Cancer Res. 2013, 19(13), 3520-3532.
Brasca MG, et al. Bioorg Med Chem. 2013, 21(22), 7047-7063.