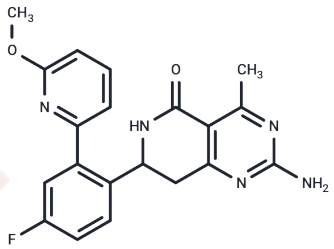
Data Sheet (Cat.No.T6118)

TargetMol

NVP-HSP990

Chemical Properties



CAS No. : 934343-74-5

Formula: C20H18FN5O2

Molecular Weight: 379.39

Storage: Store at low temperature
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	NVP-HSP990 (HSP990) is an effective and specific HSP90α/β inhibitor (IC50: 0.6 /0.8 nM).
Targets(IC50)	Apoptosis,HSP
In vitro	NVP-HSP990 is based on a 2-amino-4-methyl-7,8-dihydropyrido[4,3-d]pyrimidin-5(6H)-one scaffold, which is structurally distinct from other known HSP90 inhibitors. NVP-HSP990 binds to the N-terminal ATP-binding domain of HSP90. NVP-HSP990 exhibits single digit nanomolar IC50 values on three of the HSP90 isoforms (HSP90α, HSP90β, and GRP94) and 320 nM IC50 value on the fourth (TRAP-1), with selectivity against unrelated enzymes, receptors, and kinases. NVP-HSP990 dissociates the HSP90-p23 complex, depleted client protein c-Met, and induced Hsp70 in c-Met amplified GTL-16 gastric tumor cells. NVP-HSP990 potently inhibites the growth of human cell lines and primary patient samples from a variety of tumor types. [1] NVP-HSP990 displays dose- and time-dependent effects on HSP90 client proteins. NVP-HSP990 inhibits Glioma tumor-initiating cells (GIC) proliferation in all GIC lines, with IC50 values ranging approximately between 10 and 500 nM. Olig2 is a functional marker associated with cell proliferation and response to NVP-HSP990, as NVP-HSP990 attenuated cell proliferation in Olig2-high GIC lines. In addition, NVP-HSP990 disrupted cell-cycle control mechanism by decreasing CDK2 and CDK4 and elevating apoptosis-related molecules. [2]
In vivo	NVP-HSP990 exhibits drug-like pharmaceutical and pharmacologic properties with high oral bioavailability. In the GTL-16 xenograft model, a single oral administration of 15 mg/kg of NVP-HSP990 induced sustained downregulation of c-Met and upregulation of Hsp70. In repeat dosing studies, NVP-HSP990 treatment resulted in tumor growth inhibition of GTL-16 and other human tumor xenograft models driven by well-defined oncogenic HSP90 client proteins. [1]
Kinase Assay	HSP90 binding, ATPase, and selectivity profiling assays: The potency of HSP90 inhibitors for HSP90α, HSP90β, and Grp94 is determined by AlphaScreen competition binding assays, and activity against TRAP-1 is assessed by an ATPase assay.
Cell Research	Dissociated GICs are plated at 10 cells/μL in 6-well plates and incubated with various concentrations of NVP-HSP990 for 7 days. Formed tumorspheres are dissociated into single cells and counted with hemocytometer using 0.2% Trypan blue exclusion. (Only for Reference)

Solubility Information

Solubility	Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 36.25 mg/mL (95.55 mM),Sonication is recommended. 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: 2 mg/mL (5.27 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 vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.6358 mL	13.1791 mL	26.3581 mL
5 mM	0.5272 mL	2.6358 mL	5.2716 mL
10 mM	0.2636 mL	1.3179 mL	2.6358 mL
50 mM	0.0527 mL	0.2636 mL	0.5272 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

Menezes DL, et al. Mol Cancer Ther, 2012, 11(3), 730-739.
Fu J, et al. Cancer Res, 2013, 73(10), 3062-3074.