NVP-BAG956

Cat. No.: HY-13333

CAS No.: 853910-02-8

Molecular Formula: $C_{28}H_{21}N_5$

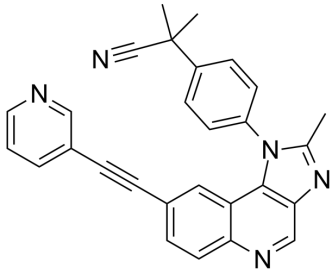
Molecular Weight: 427.5

Target: PI3K

Pathway: PI3K/Akt/mTOR

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 : 50 mg/mL (116.96 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3392 mL	11.6959 mL	23.3918 mL
	5 mM	0.4678 mL	2.3392 mL	4.6784 mL
	10 mM	0.2339 mL	1.1696 mL	2.3392 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 (5.85 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.85 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.85 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

NVP-BAG956 is an ATP-competitive PI3K inhibitor with IC50s of 34, 56, 112 and 444 nM for PI3Kδ, PI3Kα, PI3Kγ and PI3Kβ, respectively.

IC_{50} & Target

PI3Kδ 35 nM (IC_{50})	PI3Kα 56 nM (IC_{50})	PI3Kγ 117 nM (IC_{50})	PI3Kβ 446 nM (IC_{50})
PDK1 240 nM (IC_{50})	VEGFR1 2.56 μM (IC_{50})		

In Vitro	NVP-BAG956 also inhibits PDK1 with an IC_{50} of 240/260 nM. NVP-BAG956 also inhibits VEGFR1 with an IC_{50} of 2.56±0.56 μM. NVP-BAG956 blocks phosphorylation of PKB/Akt in A2058 cells with an IC_{50} value of 67±25 nM. Inhibition of PKB/Akt phosphorylation correlated with loss of A2058 cell proliferation for NVP-BAG956 (IC_{50}=290±20 nM). In the presence of NVP-BAG956, A2058 cells are only able to exit G2-M and then remain in G1. The $p27^{Kip1}$ expression is clearly induced by NVP-BAG956 in A2058 cells but not in C32 cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	One day after plating (7×10^3 cells/cm^2), melanoma cells (A2058, B16F1, B16F10, C32, HBL, Malme, Malme3M, NA8, SKMel2, SKMel23, A375, Hs294T, WM35, and 1205lu cells) are exposed to LY294002 (25 μM), Wortmannin (500 nM), NVP-BAG956 (1 μM) , NVP-BBD130 (1 μM), NVP-BEZ235 (1 μM), and ZSTK474 (1 μM), and Rapamycin (100 nM). Compound concentrations are set 2 log units above the IC_{50} in vitro to ensure full PI3K inhibition, except for the μM inhibitor LY294002. Cells are trypsinized and counted, and the volume is quantified using a Casy Counter and Analyser. To determine the nuclear volume, cells are resuspended in CASYton containing 0.5% Triton X-100, followed by repetitive pipetting (8×), before volume measurements[1] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Marone R, et al. Targeting melanoma with dual phosphoinositide 3-kinase/mammalian target of rapamycin inhibitors. Mol Cancer Res. 2009 Apr;7(4):601-13.

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