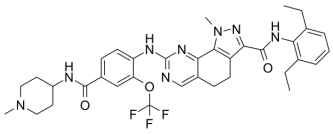
NMS-P715

Cat. No.:	HY-12382
CAS No.:	1202055-32-0
Molecular Formula:	$C_{35}H_{39}F_3N_8O_3$
Molecular Weight:	676.73
Target:	Mps1
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 2 mg/mL (2.96 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.4777 mL	7.3885 mL	14.7769 mL
	5 mM	---	---	---
	10 mM	---	---	---

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 0.5% CMC/saline water
   Solubility: 3.33 mg/mL (4.92 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

NMS-P715 is a selective, ATP-competitive inhibitor of MPS1, with an IC_{50} of 182 nM.

IC_{50} & Target

Mps1	CK2	MELK	NEK6
182 nM (IC_{50})	5.7 μM (IC_{50})	6.01 μM (IC_{50})	6.02 μM (IC_{50})

In Vitro

NMS-P715 is a selective inhibitor of MPS1, with an IC_{50} of 182 nM. NMS-P715 is highly specific for MPS1, with no other kinases inhibited below an IC_{50} value of 5 μM and only 3 kinases inhibited below 10 μM (CK2, MELK, and NEK6). NMS-P715 promotes massive spindle assembly checkpoint (SAC) override with an EC_{50} of 65 nM. NMS-P715 (1 μM) causes mitotic acceleration in U2OS cells overexpressing YFP-α-tubulin, induces aneuploidy and inhibits the proliferation of HCT116 cells. NMS-P715 (0.5, 1 μM) affects mitotic checkpoint complex (MCC) stability and cdc20 ubiquitylation[1]. NMS-P715 (1 μM) exhibits bypass of the spindle assembly checkpoint and apoptosis in pancreatic ductal adenocarcinoma (PDAC) cell lines. NMS-P715 (0-25 μM) also selectively inhibits growth of PDAC cells[2].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	NMS-P715 (10 mg/kg) exhibits an oral bioavailability of 37% and good pharmacokinetic properties in nude mice bearing subcutaneous implanted human tumor cell xenografts. NMS-P715 (90 mg/kg, p.o.) is well tolerated and cuases no signs of body weight loss or other overt toxicities in an A2780 ovary carcinoma xenograft model. NMS-P715 (100 mg/kg, p.o.) inhibits the tumor growth by appr 43% in the A375 melanoma xenograft model[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	The potency of the compound towards MPS1 and 60 additional kinases belonging to kinase selectivity screening (KSS) panel is determined using either a strong anion exchanger based assay or P81 Multiscreen plate. MPS1 activity is measured using 5 nM of MPS1 recombinant protein in 50 mM HEPES pH 7.5, 2.5 mM $MgCl_2$, 1 mM $MnCl_2$, 1 mM DTT, 3 μM $NaVO_3$, 2 mM β-glycerophosphate, 0.2 mg/mL BSA, 200 μM P38-βtide substrate-peptide (KRQADEEMTGYVATRWYRAE) and 8 μM ATP with 1.5 nM ^{33}P-γ-ATP. The assay is run in a robotized format, 10 serial 1:3 compounds dilutions (including NMS-P715, from 30 μM to 1.5 nM) are tested and IC_{50} determined[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Cells lines are seeded in 384 well-plates in the appropiate complete medium and treated with compounds (NMS-P715, etc.) dissolved in 0.1% DMSO 24 hours after seeding. The cells are incubated at 37°C and 5% CO_2 and after 72 hours the plates are processed using CellTiter-Glo assay. Inhibitory activity is evaluated comparing treated versus control data using Assay Explorer software. IC_{50} of proliferation is calculated using sigmoidal interpolation curve fitting. Activity Ratio is calculated as the ratio of the single cell line IC_{50} and the IC_{50} average of all the cell lines tested[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Athymic nu-nu mice, 5-6 weeks of age (20-22 g) are used in the assay. A2780 ovary carcinoma and A375 melanoma cells are transplanted s.c. into female nu-nu mice. Mice bearing a palpable tumor (100-200 mm^3) are selected and randomized into control and treated groups. Treatment starts one day after randomization. NMS-P715 is typically administered by oral administration at doses of 90-100 mg/kg daily for more than seven days. Each group includs 8 animals. Tumor dimension is measured regularly by calipers during the experiments and tumor mass is calculated[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Colombo R, et al. Targeting the mitotic checkpoint for cancer therapy with NMS-P715, an inhibitor of MPS1 kinase. Cancer Res. 2010 Dec 15;70(24):10255-64.

[2]. Slee RB, et al. Selective inhibition of pancreatic ductal adenocarcinoma cell growth by the mitotic MPS1 kinase inhibitor NMS-P715. Mol Cancer Ther. 2014 Feb;13(2):307-315.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA