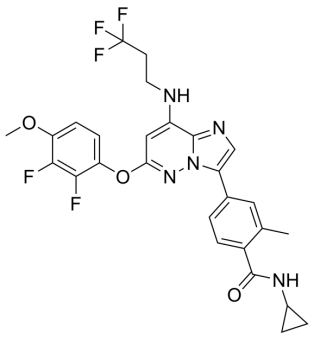
BAY1217389

Cat. No.:	HY-12859
CAS No.:	1554458-53-5
Molecular Formula:	$C_{27}H_{24}F_5N_5O_3$
Molecular Weight:	561.5
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 : ≥ 100 mg/mL (178.09 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7809 mL	8.9047 mL	17.8094 mL
5 mM	0.3562 mL	1.7809 mL	3.5619 mL
10 mM	0.1781 mL	0.8905 mL	1.7809 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 (4.45 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.45 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BAY 1217389 is a potent, and selective inhibitor of the monopolar spindle 1 (MPS1) kinase with an IC_{50} value less than 10 nM.

IC_{50} & Target

Mps1

0.63 nM (IC_{50})

In Vitro

BAY 1217389 inhibits Mps1 kinase activity with IC_{50} value below 10 nM while showing an excellent selectivity profile. In cellular mechanistic assays BAY 1217389 abrogates nocodazole-induced SAC activity and induces premature exit from mitosis resulting in multinuclearity and tumor cell death. BAY 1217389 efficiently inhibits tumor cell proliferation in vitro[1].

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

In Vivo	BAY 1217389 achieves moderate efficacy in monotherapy in tumor xenograft studies. However, in line with its unique mode of action, when combines with paclitaxel, low doses of Mps1 inhibitor reduces paclitaxel-induced mitotic arrest in line with weakening of SAC activity. As a result, combination therapy strongly improves efficacy over paclitaxel or Mps1 inhibitor monotreatment at the respective MTDs in a broad range of xenograft models including those showing acquired or intrinsic paclitaxel-resistance. BAY 1217389 shows good tolerability without adding toxicity to paclitaxel monotherapy[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Inhibition of recombinant human Mps1 by BAY 1161909 or BAY 1217389 is assessed in TRFRET-based in vitro kinase assays via phosphorylation of a biotinylated peptide (Biotin-Ahx-PWDPDDADITEILG-NH2). Under standard assay conditions kinase and test compound are preincubated for 15 min before enzyme reaction is started by addition of substrate and ATP upon 10 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Cells are seeded into 96 well plates at densities ranging from 1,000 to 5,000 cells per well in the appropriate medium supplemented with 10% FCS. After 24 hours, cells are treated in quadruplicates with serial dilutions of BAY 1161909 or BAY 1217389. After further 96 hours, adherent cells are fixed with glutaraldehyde and stained with crystal violet. IC_{50} values are calculated by means of a 4 parameter fit[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: For tumor xenograft studies female athymic NMRI nu/nu mice, 50 days old, average body weight 20-22 g, are used. When tumors reaches a size of approximately 20-40 mm^2, depending on growth of the tumor model, animals are randomized to treatment and control groups (8-10 mice / group) and treated p.o. with vehicle (70% polyethylene glycol 400, 5% Ethanol, 25% Solutol), BAY 1161909, BAY 1217389, and/or paclitaxel. For analysis of polyploidy and multinuclearity induction in vivo, A2780cis tumor bearing female NMRI nude mice are treated with paclitaxel (i.v. once with 24 mg/kg), BAY 1161909 p.o.twice daily for 2 days with 2.5 mg/kg and in combination with paclitaxel (i.v. once 24 mg/kg) and BAY 1161909 (p.o. twice daily for 2 days 1 mg/kg)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Mol Cancer. 2023 Jul 13;22(1):110.
- Cell Death Dis. 2022 Oct 13;13(10):868.
- bioRxiv. 2021 Feb 5.

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REFERENCES

[1]. Wengner AM, et al. Novel Mps1 Kinase Inhibitors with Potent Antitumor Activity. Mol Cancer Ther. 2016 Apr;15(4):583-92.

[2]. Wengner AM, et al. Novel Mps1 Kinase Inhibitors with Potent Antitumor Activity. Mol Cancer Ther. 2016 Apr;15(4):583-92.. . . .

Caution: Product has not been fully validated for medical applications. For research use only.

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