

Product Data Sheet

Product Name: BAY1217389

Cat. No.: GC19058

Chemical Properties

Cas. No. 1554458-53-5

SMILES O=C(NC1CC1)C2=CC=C(C3=CN=C4C(NCCC(F)(F)F)=CC(OC5=CC=C(OC)C(F)=C5F)=NN43)C=C2C

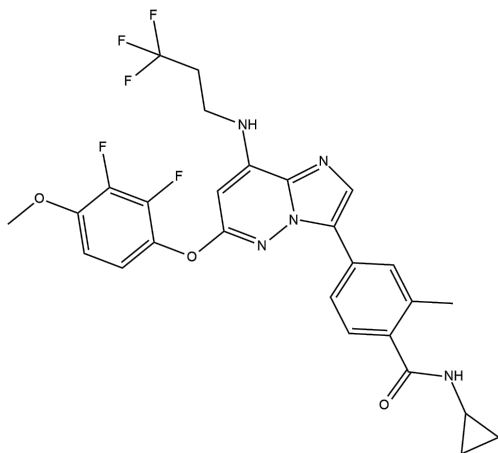
Formula $C_{27}H_{24}F_5N_5O_3$ M.Wt 561.5

Solubility DMSO : ≥ 28 mg/mL (49.87 mM) Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Kinase experiment:

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].

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

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Cell experiment: 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. IC50 values are calculated by means of a 4 parameter fit[1].

Animal experiment: 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 mm², 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].

References:

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

Background

BAY 1217389 is a potent, and selective inhibitor of the monopolar spindle 1 (MPS1) kinase with an IC50 value less than 10 nM.

BAY 1217389 inhibits Mps1 kinase activity with IC50 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].

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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].

References:

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

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