

Product Data Sheet

Product Name: Mps1-IN-1

Cat. No.: GC11292

Chemical Properties

Cas. No. 1125593-20-5

Chemical Name 1-(4-((4-((2-(isopropylsulfonyl)phenyl)amino)-1H-pyrrolo[2,3-b]pyridin-6-yl)amino)-3-methoxyphenyl)piperidin-4-ol

SMILES OC1CCN(C2=CC(OC)=C(NC3=NC4=C(C=CN4)C(NC5=C(S(=O)(C(C)C)=O)C=CC=C5)=C3)C=C2)CC1

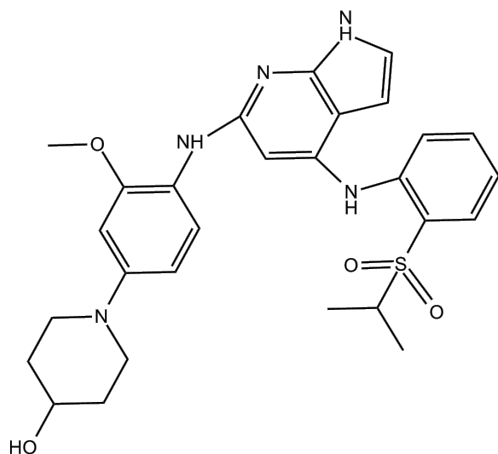
Formula $C_{28}H_{33}N_5O_4S$ M.Wt 535.66

Solubility $\geq 16.05\text{mg/mL}$ in DMSO 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

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

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**Kinase
experiment:**

The kinase binding assay is used to assess compound binding to TTK by monitoring displacement of a fluorescently labeled, ATP site-directed kinase inhibitor (Kinase Tracer 236) from the kinase active site. Each 15 μ L assay contains 5 nM TTK, variable amounts of test compound (Mps1-IN-1), 30 nM Kinase Tracer 236, 2 nM Eu-anti-GST Antibody, and 1% DMSO (residual from compound dilution) in Kinase Buffer A (50 mM HEPES pH 7.5, 10 mM MgCl₂, 1 mM EGTA, 0.01% Brij-35). Binding assays are initiated by addition of 5 μ L of test compound (from 2-fold dilution series) to 5 μ L of a kinase/antibody mixture, followed by addition of 5 μ L of antibody. Assay plates are read using standard Eu-based TR-FRET settings with excitation at 340 nm and emission monitored at 615 nm (donor) and 665 nm (acceptor). Emission intensities are measured over a 200 μ s window following a 100 μ s post-excitation delay[1].

Cell experiment: U2OS cells expressing doxycycline-inducible PLK4 are plated in 96 well plates. A double thymidine block is performed using the following treatment regimen: thymidine for 18-20 hrs., release for 10 hrs. with doxycycline induction of PLK4 during this time, then a second thymidine block, followed by release. Six hours after the 2nd thymidine release, Mps1-IN-1 (or DMSO vehicle) is added and the proliferation of the cell populations is monitored with Cell Titer GLO assay[1].

References:

[1]. Kwiatkowski N, et al. Small-molecule kinase inhibitors provide insight into Mps1 cell cycle function. Nat Chem Biol. 2010 May;6(5):359-68.

Background

Mps1-IN-1 is a selective Mps1 (monopolar spindle 1) kinase inhibitor with IC₅₀ value of 367 nM.

MPS1 (monopolar spindle 1 kinase) is a crucial part of the spindle assembly checkpoint. It facilitates the formation of C-MAD2 (closed MAD2) conformer and the MCC (mitotic checkpoint complex) assembly, involved in the maintenance of chromosomal stability and tumor growth.

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Mps1-IN-1 abolishes the SAC (spindle assembly checkpoint) function. In U2OS cells, dose-dependent treatment of Mps1-IN-1 decreases the time spent in mitosis with almost 100% cells starting anaphase in 20 minutes. In contrast, just 10% of DMSO-treated cells starting anaphase in the same period. Acceleration of mitosis kinetics in Mps1-IN-1 treated cells affects genomic stability and causes aneuploidy. In addition, Mps1-IN-1 treated cells shows decrease in kinetochore-bound Mad2 by 80%. Mps1-IN-1-treated cells spent roughly 40% less time in mitosis as compared to DMSO-treated cells. Moreover, Mps1-IN-1 disrupts the kinase activity of Aurora B. Mps1-IN-1 treatment lead to decrease in the phosphorylation status of Aurora B at Thr232 in a dose-dependent manner. Furthermore, Mps1-IN-1 increases multipolar cell divisions and decreases cell viability.

Reference:

[1].Kwiatkowski N, Jelluma N, Filippakopoulos P et al. Small-molecule kinase inhibitors provide insight into Mps1 cell cycle function. Nat Chem Biol. 2010 May;6(5):359-68.

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