

Product Data Sheet

Product Name: GSK-923295

Cat. No.: GC15659

Chemical Properties

Cas. No. 1088965-37-0

Chemical Name 3-chloro-N-[(2S)-1-[[2-(dimethylamino)acetyl]amino]-3-[4-[8-[(1S)-1-hydroxyethyl]imidazo[1,2-a]pyridin-2-yl]phenyl]propan-2-yl]-4-propan-2-yloxybenzamide

SMILES CC(C)OC1=C(C=C(C=C1)C(=O)NC(CC2=CC=C(C=C2)C3=CN4C=CC=C(C4=N3)C(C)O)CNC(=O)CN(C)C)Cl

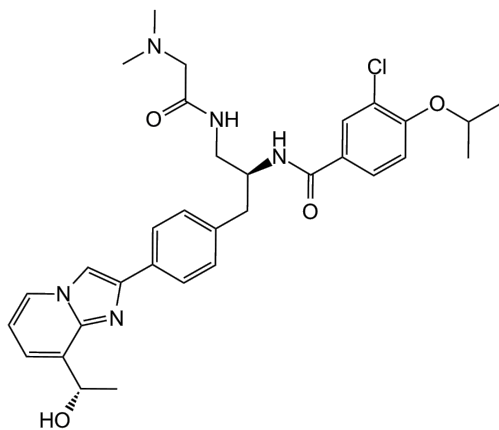
Formula $C_{32}H_{38}ClN_5O_4$ M.Wt 592.14

Solubility $\geq 29.6\text{mg/mL}$ 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

Kinase experiment [1]:

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Enzymology

Kinesin motor domains were expressed in Escherichia coli BL21 (DE3) and purified. CENP-E proteins included residues 2 ~ 340 with a carboxyl-terminal 6-his tag. All studies using MT were conducted in PEM25 buffer [25 mM PipesK+ (pH 6.8), 2 mM MgCl₂, 1 mM EGTA] supplemented with 10 μ M Paclitaxel. The IC₅₀ for steady-state inhibition was determined at 500 μ M ATP, 5 μ M MT and 1 nM CENP-E in PEM25 buffer.

Cell experiment [1]:

Cell lines

Tumor cell lines

Preparation method

The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37°C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reaction Conditions~ 10 μ M; 72 hrs

Applications

In 237 tumor cell lines, GSK92329 potently inhibited tumor cell growth, with an average GI₅₀ of 253 nM and a median GI₅₀ of 32 nM.

Animal experiment [1]:

Animal models

Mice bearing Colo205 xenografts

Dosage form

125 mg/kg; i.p.; 2 cycles of 3 daily injections separated by 1 week

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Applications GSK923295 exhibited robust and dose-dependent antitumor activity against Colo205 xenografts, including partial and complete regressions at the dose of 125 mg.

Other notes Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

[1]. Wood K W et al. , Antitumor activity of an allosteric inhibitor of centromere-associated protein-E. 2010, 107 (13): 5839-5844.

Background

GSK923295 is a specific inhibitor of CENP-E kinesin motor with IC50 value of 3.2 nM [1].

Centromere-associated protein E (CENP-E) is a mitotic kinesin, which is the connect of mitosis process with the mitotic checkpoint signaling. It Interacts with spindle microtubules and contribute to the chromosome alignment, and thus it regulates the cell-cycle transition from metaphase to anaphase.

When asynchronous cultured cells were exposed to GSK923295, the penetrant cell-cycle delay in mitosis was observed, which accompanied with morphological changes similar to RNAi-mediated knockdown of CENP-E mRNA. It indicated a significant inhibition of CENP-E by GSK923295. In the presence of GSK9232195, CENP-E microtubule (MT)-stimulated ATPase showed a dramatic slowing of release of ADP and Pi, where the ATP-bound form was stabilized and the activity of CENP-E was inhibited. This observation suggested GSK923295 inhibited CENP-E via the suppression of MT-stimulated ATPase [1].

In mouse model, mice bearing xenografts of the Colo205 colon tumor cell line were administered with GSK923295 of 125 mg/kg. The result showed GSK923295-induced cell-cycle changes of tumor cells and increased scattered apoptosis body. Additionally, long-term study via measuring tumor volume

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revealed significant antitumor activity of GSK923295, in a manner of dose-dependent [1].

Reference:

[1] Wood K W et al. , Antitumor activity of an allosteric inhibitor of centromere-associated protein-E. 2010, 107 (13): 5839-5844.

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