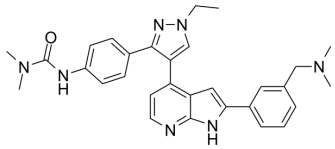
GSK-1070916

Cat. No.:	HY-70044
CAS No.:	942918-07-2
Molecular Formula:	$C_{30}H_{33}N_7O$
Molecular Weight:	507.63
Target:	Aurora Kinase; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Epigenetics; Apoptosis
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 : 16.67 mg/mL (32.84 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9699 mL	9.8497 mL	19.6994 mL
	5 mM	0.3940 mL	1.9699 mL	3.9399 mL
	10 mM	0.1970 mL	0.9850 mL	1.9699 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: ≥ 1.67 mg/mL (3.29 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.67 mg/mL (3.29 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1 mg/mL (1.97 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK-1070916 is a potent and selective ATP-competitive inhibitor of aurora B and aurora C with K_is of 0.38 and 1.5 nM, respectively, and is >250- fold selective over Aurora A.

IC_{50} & Target

Aurora B	Aurora C
0.38 nM (Ki)	1.5 nM (Ki)

In Vitro

GSK-1070916 potently inhibits Aurora B/INCENP and Aurora C/INCENP kinases with K_is of 0.38±0.29 and 1.45±0.35 nM,

	respectively, but is less potent against Aurora A/ TPX2 with a K_i of 492±61 nM. GSK-1070916 also inhibits FLT1, TIE2, SIK, FLT4, and FGFR1 with IC_{50} values of 42, 59, 70, 74, and 78 nM, respectively. Treatment of A549 human lung cancer cells with GSK-1070916 results in a potent antiproliferative effect (EC_{50}=7 nM)[1]. GSK-1070916 inhibits a panel of tumor cell lines and is shown o inhibits the phosphorylation of HH3- S10 in all cell lines with average EC_{50} values ranging from 8 to 118 nM[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In nude mice implanted with human colon tumor (HCT116) xenografts, a single dose of GSK-1070916 administered i.p. inhibits HH3-S10 phosphorylation in a dose-dependent manner. Repeated i.p. administration of GSK-1070916 produces complete or partial antitumor activity in 4 of 8 tumor types [lung, A549; colon, HCT116; acute myelogenous leukemia (AML), HL60; and chronic myelogenous leukemia, K562], stable disease in 3 of 8 (colon, Colo205; lung, H460; and breast, MCF-7), and tumor growth delay in 1 of 8 tumor types (colon, SW620). Daily administration of GSK-1070916 is generally well-tolerated[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	A panel of tumor cell lines are plated in 96-well plates in the recommended growth media and incubated at 37°C in 5% CO_2 overnight. The following day, the cells are treated with serial dilutions of GSK-1070916. At this time, one set of cells is treated with CellTiter-Glo for a time equal to 0 (T=0) measurement. Following a 6- to 7-d incubation with compound, cell proliferation is measured using the CellTiter-Glo reagent[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice: Tumors are initiated by injection of tumor cell suspensions (A549, SW620, HCT116, H460, MCF-7, HL60, K562) or tumor fragments (Colo205) s.c. into nude (A549, SW620, HCT116, H460, MCF-7, HL60, and Colo205) or severe combined immunodeficient (SCID; K562) mice. When the tumors reach a volume of 80 to 200 mm^3, the mice are randomized into groups of 5 to 10 mice per group. GSK-1070916 is administered at 25, 50, or 100 mg/kg once daily for 5 consecutive days-on, 2d-off, schedule for two (Colo205 and HL60) or three (A549, SW620, HCT116, H460, MCF-7, K562) cycles. Tumors are measured twice weekly[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- J Biomol Screen. 2013 Oct;18(9):1062-71.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Adams ND, et al. Discovery of GSK-1070916, a potent and selective inhibitor of Aurora B/C kinase. J Med Chem. 2010 May 27;53(10):3973-4001.

[2]. Hardwicke MA, et al. GSK-1070916, a potent Aurora B/C kinase inhibitor with broad antitumor activity in tissue culture cells and human tumor xenograft models. Mol Cancer Ther. 2009 Jul;8(7):1808-17.

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

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