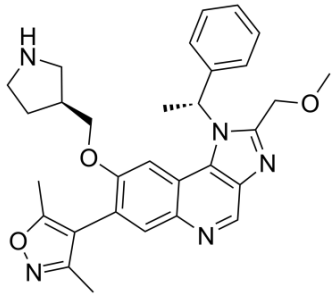
GSK778

Cat. No.:	HY-136570
CAS No.:	2451862-42-1
Molecular Formula:	$C_{30}H_{33}N_5O_3$
Molecular Weight:	511.61
Target:	Epigenetic Reader Domain; Apoptosis
Pathway:	Epigenetics; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 41.67 mg/mL (81.45 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9546 mL	9.7731 mL	19.5461 mL
	5 mM	0.3909 mL	1.9546 mL	3.9092 mL
	10 mM	0.1955 mL	0.9773 mL	1.9546 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: ≥ 2.08 mg/mL (4.07 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (4.07 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.07 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK778 (iBET-BD1) is a potent and selective BD1 bromodomain inhibitor of the BET proteins, with IC_{50}s of 75 nM (BRD2 BD1), 41 nM (BRD3 BD1), 41 nM (BRD4 BD1), and 143 nM (BRDT BD1), respectively. GSK778 phenocopies the effects of pan-BET inhibitors in cancer models[1].

IC_{50} & Target	BRD2 BD1	BRD3 BD1	BRD4 BD1	BRDT BD1
	75 nM (IC_{50})	41 nM (IC_{50})	41 nM (IC_{50})	143 nM (IC_{50})

In Vitro

GSK778 inhibits BRD BD2 with the IC_{50}s of 3950 nM (BRD2 BD2), 1210 nM (BRD3 BD2), 5843 nM (BRD4 BD2), and 17451 nM (BRDT BD2), respectively[1].

GSK778 (0.01-10 μM; 72 hours) inhibits the proliferative activity of human primary $CD4^+$ T cells and the production of effector cytokines including IFNγ, IL-17A and IL-22[1].

GSK778 (0.001-10 μM; 5 days) has a more pronounced effect on the growth and viability of MDA-453, MOLM-13, K562, MV4-11, THP-1, and MDA-MB-231 cells[1].

GSK778 (1000 nM; 72 hours) inhibits proliferation, induces a cell cycle arrest and apoptosis in MV4-11, MOLM13, MDA-MB-231 and MB453 cells[1].

GSK778 (1000 nM; 12 days) reduces the clonogenic capacity of primary human AML cells[1].

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

Cell Proliferation Assay[1]

Cell Line:	Human primary $CD4^+$ T cell
Concentration:	0.001, 0.01, 0.1, 1, 10 μM
Incubation Time:	72 hours
Result:	Inhibited the proliferative activity of the cells and the production of effector cytokines.

Cell Viability Assay[1]

Cell Line:	MDA-453, MOLM-13, K562, MV4-11, THP-1, and MDA-MB-231 cells
Concentration:	0.001, 0.01, 0.1, 1, 10 μM
Incubation Time:	5 days
Result:	Inhibited the growth and viability of human cancer cell lines.

Apoptosis Analysis[1]

Cell Line:	MV4-11, MOLM13, MDA-MB-231 and MB453 cells
Concentration:	1000 nM
Incubation Time:	72 hours
Result:	Inhibited cell proliferation and induced a cell cycle arrest and apoptosis.

In Vivo

GSK778 (15 mg/kg/BID; i.p. for 30 days) offers a superior survival advantage to iBET-BD2 in the aggressive MLL-AF9 AML model[1].

GSK778 (15 mg/kg/BID; s.c. for 14 days) reduces the production of anti-keyhole limpet hemocyanin (KLH) IgM and is well tolerated[1].

GSK778 exhibits C_{max} (85 ng/mL), T_{max} (1.48 h) and AUC_{∞} (132 ng.h/mL) following oral administration (10 mg/kg) in mice[1].

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

Animal Model:	6-8 weeks female C57BL/6 mice are injected with MLL-AF9 cells[1]
Dosage:	15 mg/kg/BID
Administration:	I.p. injections for 30 days
Result:	Increased the survival rate of leukemia mice.

Animal Model:	Male CD1 mice[1]
Dosage:	10 mg/kg (Pharmacokinetic Analysis)
Administration:	P.o. administration
Result:	C_{max} (85 ng/mL), T_{max} (1.48 h); AUC_{∞} (132 ng.h/mL).

REFERENCES

[1]. Omer G, et, al. Selective targeting of BD1 and BD2 of the BET proteins in cancer and immunoinflammation. Science. 2020 Apr 24; 368(6489): 387-394.

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