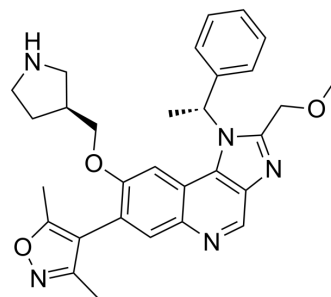


GSK778

Cat. No.:	HY-136570		
CAS No.:	2451862-42-1		
Molecular Formula:	C ₃₀ H ₃₃ N ₅ O 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	1 year
		-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro	DMSO : 41.67 mg/mL (81.45 mM; Need ultrasonic)			
		Solvent Concentration	Mass	
			1 mg	5 mg
			10 mg	
Preparing Stock Solutions	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	<ol style="list-style-type: none"> 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 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 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] .			
IC₅₀ & Target	BRD2 BD1 75 nM (IC ₅₀)	BRD3 BD1 41 nM (IC ₅₀)	BRD4 BD1 41 nM (IC ₅₀)	BRDT BD1 143 nM (IC ₅₀)

In Vitro

GSK778 inhibits BRD BD2 with the IC₅₀s of 3950 nM (BRD2 BD2), 1210 nM (BRD3 BD2), 5843 nM (BRD4 BD2), and 17451 nM (BRD5 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 IFN γ , 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.

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

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