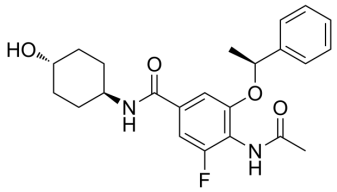
GSK046

Cat. No.:	HY-136571
CAS No.:	2474876-09-8
Molecular Formula:	$C_{23}H_{27}FN_2O_4$
Molecular Weight:	414.47
Target:	Epigenetic Reader Domain
Pathway:	Epigenetics
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 : 83.33 mg/mL (201.05 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4127 mL	12.0636 mL	24.1272 mL
5 mM	0.4825 mL	2.4127 mL	4.8254 mL
10 mM	0.2413 mL	1.2064 mL	2.4127 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 (5.02 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.02 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.02 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK046 (iBET-BD2) is a potent, selective and orally active BD2 bromodomain inhibitor of the BET proteins, with IC_{50}s of 264 nM (BRD2 BD2), 98 nM (BRD3 BD2), 49 nM (BRD4 BD2) and 214 nM (BRDT BD2), respectively. GSK046 has immunomodulatory activity[1].

IC_{50} & Target

BRD2 BD2	BRD3 BD2	BRD4 BD2	BRDT BD2
264 nM (IC_{50})	98 nM (IC_{50})	49 nM (IC_{50})	214 nM (IC_{50})

In Vitro

GSK046 (1000 nM; refresh every three days) reduces the recruitment of BET proteins to interferon (IFN) target genes following IFN-γ stimulation. GSK046 appears to more prominently affect the recruitment of BRD2 and BRD3 compared to BRD4[1].

GSK046 (0.1-10 μM) displays a more selective phenotypic fingerprint, particularly inhibiting the production of key pro-inflammatory mediators including Th17 cytokines in the B and T cell co-culture system[1].

GSK046 (0.01-10 μM; 72 hours) does not affect the proliferative activity of human primary $CD4^+$ T cells but still inhibits the production of effector cytokines including IFNγ, IL-17A and IL-22[1].

GSK046 (0.005-10 μM; 48 hours) impairs macrophage activation following PMA stimulation, without impacting cellular viability[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:	Did not affect the proliferative activity of the cells but still inhibited the production of effector cytokines.

In Vivo

GSK046 (40 mg/kg/QD; s.c. for 14 days) has immunomodulatory activity[1].

GSK046 exhibits C_{max} (C57BL6 1589, C57B16 2993 ng/mL) and terminal elimination half-lives (C57BL6 1.8, C57B16 1.9 h) following oral administration (C57BL6 10, C57B16 40 mg/kg)[1].

GSK046 exhibits C_{max} (mouse 1589, rat 202 ng/mL) and terminal elimination half-lives (mouse 1.8, rat 1.4 h) following oral administration (mouse 10, rat 10 mg/kg)[1].

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

Animal Model:	Male C57BL/6 mice (8/10-weeks-old) are injected with keyhole limpet hemocyanin (KLH)[1]
Dosage:	40 mg/kg/QD
Administration:	S.c. injections for 14 days
Result:	Reduced the production of anti-keyhole limpet hemocyanin (KLH) IgM and was well tolerated.

Animal Model:	Female C57BL/6 mice[1]
Dosage:	10 mg/kg (Pharmacokinetic Analysis)
Administration:	Oral administration
Result:	C_{max} (1859 ng/mL), $T_{1/2}$ (1.8 h).

Animal Model:	Male C57BL/6 mice[1]
Dosage:	40 mg/kg (Pharmacokinetic Analysis)
Administration:	Oral administration
Result:	C_{max} (2993 ng/mL), $T_{1/2}$ (1.9 h).

Animal Model:	Female Lewis rat[1]
Dosage:	10 mg/kg (Pharmacokinetic Analysis)
Administration:	Oral administration
Result:	C_{max} (202 ng/mL), $T_{1/2}$ (1.4 h).

CUSTOMER VALIDATION

- iScience. 17 October 2022, 105376.
- Cell Signal. 2021 Dec 30;110226.

See more customer validations on www.MedChemExpress.com

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.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA