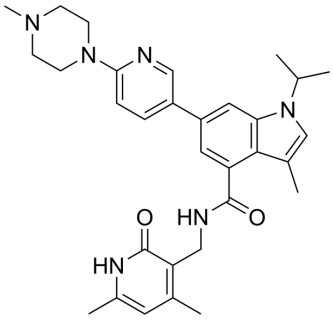
GSK503

Cat. No.:	HY-12856
CAS No.:	1346572-63-1
Molecular Formula:	$C_{31}H_{38}N_6O_2$
Molecular Weight:	526.67
Target:	Histone Methyltransferase
Pathway:	Epigenetics
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 : ≥ 44 mg/mL (83.54 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8987 mL	9.4936 mL	18.9872 mL
	5 mM	0.3797 mL	1.8987 mL	3.7974 mL
	10 mM	0.1899 mL	0.9494 mL	1.8987 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: ≥ 2.5 mg/mL (4.75 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.75 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK503 is a potent and specific inhibitor of EZH2 methyltransferase with K_i^{app} values of 3 to 27 nM.

IC_{50} & Target

EZH2

In Vitro

GSK503 inhibits the methyltransferase activity of wild type and mutant EZH2 with similar potency (K_i^{app}=3-27 nM) and is structurally related to GSK126 and GSK343. GSK503 is >200 fold selective over EZH1 (K_i^{app}=636 nM) and >4000 fold selective over other histone methyltransferases[1].

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

In Vivo	In a melanoma mouse model, conditional EZH2 ablation as much as treatment with the GSK503 stabilizes the disease through inhibition of growth and virtually abolishes metastases formation without affecting normal melanocyte biology[2]. GSK503 displays favorable pharmacokinetics in mice. GSK503, but not vehicle, prevents the formation of germinal center after SRBC or NP-KLH immunization, phenocopying the Ezh2 null phenotype. GSK503 treatment leads to reduced numbers of GC B-cells by flow cytometry, reduces number and volume of GCs by immunohistochemistry, and impairs formation high affinity antibodies[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Mice: To pharmacologically inhibit Ezh2 activity, Tyr::N-Ras^{Q61K} Ink4a$^{-/-}$ and C57Bl/6 mice are subjected to treatment with GSK503, which is diluted (15 mg/mL) in 20% Captisol solution. Efficient Ezh2 inhibition is achieved by daily intraperitoneal injections of 150 mg/kg GSK503 over 35 consecutive days. Mice are monitored during and after treatment to measure GSK503-induced reversible weight loss. C57Bl/6 and Foxn1nu/nu mice engrafted with melanoma cells are subjected to TM and GSK503 treatment as described above[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2019 Feb 19;116(8):2961-2966.
- PLoS Pathog. 2020 Mar 24;16(3):e1008429.
- Int Immunopharmacol. 2023 Sep 12;124(Pt A):110918.
- Exp Eye Res. 2023 Jan 18;227:109389.
- Patent. US20180263995A1.

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REFERENCES

[1]. Béguelin W, et al. EZH2 is required for germinal center formation and somatic EZH2 mutations promote lymphoid transformation. Cancer Cell. 2013 May 13;23(5):677-92.

[2]. Zingg D, et al. The epigenetic modifier EZH2 controls melanoma growth and metastasis through silencing of distinct tumour suppressors. Nat Commun. 2015 Jan 22;6:6051.

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

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