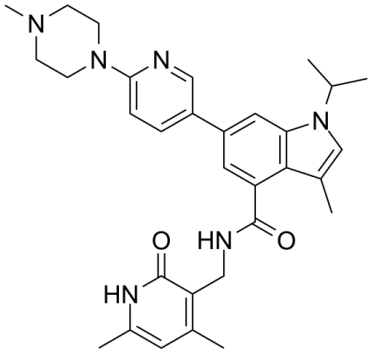
Data Sheet

Product Name:	GSK503
Cat. No.:	CS-4179
CAS No.:	1346572-63-1
Molecular Formula:	C31H38N6O2
Molecular Weight:	526.67
Target:	Histone Methyltransferase
Pathway:	Epigenetics
Solubility:	DMSO : ≥ 44 mg/mL (83.54 mM)



BIOLOGICAL ACTIVITY:

GSK503 is a potent and specific inhibitor of **EZH2** methyltransferase with **K_i^{app}** values of 3 to 27 nM. IC50 & Target: Ki: 3 to 27 nM (EZH2)[1] **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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: [2]Mouse: 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].

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.

CAIndexNames:

1H-Indole-4-carboxamide, N-[(1,2-dihydro-4,6-dimethyl-2-oxo-3-pyridinyl)methyl]-3-methyl-1-(1-methylethyl)-6-[6-(4-methyl-1-piperazinyl)-3-pyridinyl]-

SMILES:

O=C(C1=CC(C2=CC=C(N3CCN(C)CC3)N=C2)=CC4=C1C(C)=CN4C(C)C)NCC5=C(C)C=C(C)NC5=O

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

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