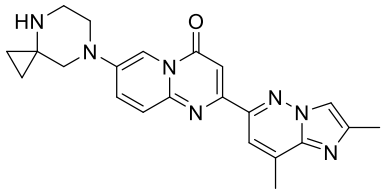
Product data sheet

MedKoo Cat#: 406635 Name: GSK-503 CAS#: 1346572-63-1 Chemical Formula: $C_{31}H_{38}N_6O_2$ Exact Mass: 526.30562 Molecular Weight: 526.67	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

GSK-503 is a potent EZH2 inhibitor with potential anticancer activity. Increased activity of the epigenetic modifier EZH2 has been associated with different cancers. In a melanoma mouse model, conditional Ezh2 ablation as much as treatment with the preclinical EZH2 inhibitor GSK503 stabilizes the disease through inhibition of growth and virtually abolishes metastases formation without affecting normal melanocyte biology. Comparably, in human melanoma cells, EZH2 inactivation impairs proliferation and invasiveness, accompanied by re-expression of tumour suppressors connected to increased patient survival. These EZH2 target genes suppress either melanoma growth or metastasis in vivo, revealing the dual function of EZH2 in promoting tumour progression. Thus, EZH2-mediated epigenetic repression is highly relevant especially during advanced melanoma progression, which makes EZH2 a promising target for novel melanoma therapies. (Nat Commun. 2015 Jan 22;6:6051. doi: 10.1038/ncomms7051.)

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	53.0	100.63
DMF	25.0	47.47
DMF:PBS (pH 7.2) (1:1)	0.5	0.95
Ethanol	3.0	5.70

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.90 mL	9.49 mL	18.99 mL
5 mM	0.38 mL	1.90 mL	3.80 mL
10 mM	0.19 mL	0.95 mL	1.90 mL
50 mM	0.04 mL	0.19 mL	0.38 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Martin-Mateos R, De Assuncao TM, Arab JP, Jalan-Sakrikar N, Yaqoob U, Greuter T, Verma VK, Mathison AJ, Cao S, Lomberk G, Mathurin P, Urrutia R, Huebert RC, Shah VH. Enhancer of Zeste Homologue 2 Inhibition Attenuates TGF-β Dependent Hepatic Stellate Cell Activation and Liver Fibrosis. Cell Mol Gastroenterol Hepatol. 2019;7(1):197-209. doi: 10.1016/j.jcmgh.2018.09.005. Epub 2018 Sep 15. PMID: 30539787; PMCID: PMC6282644.

In vivo study

1. Zhen Y, Smith RD, Finkelman FD, Shao WH. Ezh2-mediated epigenetic modification is required for allogeneic T cell-induced lupus disease. Arthritis Res Ther. 2020 Jun 5;22(1):133. doi: 10.1186/s13075-020-02225-9. PMID: 32503684; PMCID: PMC7275547.
2. Zingg D, Debbache J, Schaefer SM, Tuncer E, Frommel SC, Cheng P, Arenas-Ramirez N, Haeusel J, Zhang Y, Bonalli M, McCabe MT, Creasy CL, Levesque MP, Boyman O, Santoro R, Shakhova O, Dummer R, Sommer L. The epigenetic modifier EZH2 controls melanoma growth and metastasis through silencing of distinct tumour suppressors. Nat Commun. 2015 Jan 22;6:6051. doi: 10.1038/ncomms7051. PMID: 25609585.

7. Bioactivity

Biological target:

GSK503 is an inhibitor of EZH2 methyltransferase with Kiapp values of 3 to 27 nM.

In vitro activity

First, this study used an epigenetic compound, GSK-503, which specifically targets the catalytic subunit of EZH2. Inhibition of EZH2 in cells treated with GSK-503 and TGF-β led to a significant decrease in fibronectin, α-SMA, and collagen 1α1, both at mRNA and protein levels (Figure 3A and B). Parallel to this effect, this study confirmed a significant down-regulation of H3K27me3 measured by Western blot and immunofluorescence (Figure 3C and D).

Reference: Cell Mol Gastroenterol Hepatol. 2019; 7(1): 197–209. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6282644/

In vivo activity

The decreased severity of bm12 cGVHD when Ezh2 genetically deleted in donor T cells and previous observations that Ezh2 is upregulated in GC T and B cells suggested that pharmacological inhibition of Ezh2 might suppress lupus-like features of bm12 cGVHD. This study tested this hypothesis by evaluating the ability of GSK503, a small molecule Ezh2 inhibitor, to suppress disease in this study's cGVHD model when treatment is initiated 2 days before donor T cell injection. Mice were followed with serum levels of anti-dsDNA and anti-chromatin antibody. As expected, serum anti-dsDNA and anti-chromatin Ab levels increased in 2 weeks in bm12 host mice injected with WT, but not Ezh2-deficient CD4+ T cells (Figs. 1 and 6). Importantly, the increase in autoantibody levels in bm12 hosts injected with WT B6 CD4+ T cells was totally prevented by the GSK503 treatment (Fig. 6). These observations suggest that agents, such as GSK503, that specifically target Ezh2 may be useful for the treatment of SLE autoimmunity.

Reference: Arthritis Res Ther. 2020; 22: 133. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7275547/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.