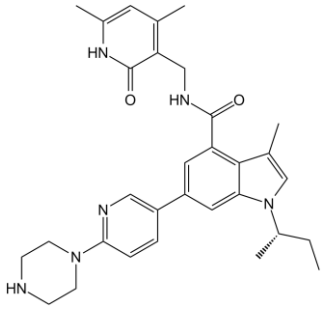
Product Data Sheet

Product Name:	GSK126
Cat. No.:	GC15783
Chemical Name:	1-[(2S)-butan-2-yl]-N-[(4,6-dimethyl-2-oxo-1H-pyridin-3-yl)methyl]-3-methyl-6-(6-piperazin-1-ylpyridin-3-yl)indole-4-carboxamide

CHEMICAL PROPERTIES

Cas No.:	1346574-57-9		
Molecular Formula:	$C_{31}H_{38}N_6O_2$		
Molecular Weight:	526.67		
Storage:	Powder	-80°C	2 years
		-20°C	1 year
	In solvent	-80°C	6 months
		-20°C	1 month
Solubility:	>3.29mg/mL in DMSO		

Chemical Structure:



Background

GSK126 is an inhibitor of EZH2 with Ki Value of 93 pM [1].

Over-expression of EZH2 has been reported to be correlated with cancer progression and poor prognosis, high grade and high stage in several tumor types. GSK126 is a potent inhibitor of EZH2 and its functional residence time on activated form of EZH2/PRC2 is mush longer than unactivated forms [1]. When tested with lymphoma cell lines, results showed that harboring EZH2 mutations such as Y641N, Y641F or A677G were more sensitivity [2]. In DMS53, Lu30, H209 SCLC cells, cellular growth was inhibited with 0.5, 2, and 8μM GSK126 treatment [3]. And GSK126 could also significantly restore ARNTL expression in ovarian cancer cells thus inhibit cell growth and enhance chemosensitivity of cisplatin [4].

Intermittent dosing of GSK126 treated subcutaneous KARPAS-422 xenografts model could effectively inhibit its growth with or without a 1 week drug holiday. In mouse model with EZH2 mutant DLBCL xenografts, treatment with GSK126 could markedly inhibit its growth [2].

References:
1. Sato, T., et al., PRC2 overexpression and PRC2-target gene repression relating to poorer prognosis in small cell lung cancer. Sci Rep, 2013. 3(1911).
2. McCabe, M.T., et al., EZH2 inhibition as a therapeutic strategy for lymphoma with EZH2-activating mutations. Nature, 2012. 492(7427): p. 108-12.
3. Van Aller, G.S., et al., Long residence time inhibition of EZH2 in activated polycomb repressive complex 2. ACS Chem Biol, 2014. 9(3): p. 622-9.
4. Yeh, C.M., et al., Epigenetic silencing of ARNTL, a circadian gene and potential tumor suppressor in ovarian cancer. Int J Oncol, 2014. 45(5): p. 2101-7.

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