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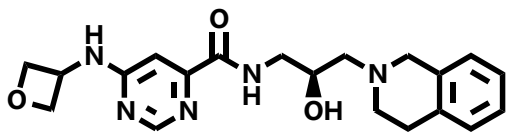
PRMT5 Inhibitor - EPZ015666 (GSK3235025)

Chemical Name: (S)-N-(3-(3,4-dihydroisoquinolin-2(1H)-yl)-2-hydroxypropyl)-6-(oxetan-3-ylamino)pyrimidine-4-carboxamide



Molecular Weight:	383.44
Formula:	$C_{20}H_{25}N_5O_3$
Purity:	≥98%
CAS#:	1616391-65-1
Solubility:	DMSO and EtOH up to 100 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

EPZ015666 is a potent, selective and orally bioavailable Protein arginine methyltransferase-5 (PRMT5) Inhibitor with Ki of 5 nM. It has >20,000-fold selectivity over other PMTs. It showed competitive inhibition with respect to the peptide substrate, not SAM. Treatment of MCL cell lines with EPZ015666 led to inhibition of SmD3 methylation and cell death, with IC_{50} values in the nanomolar range. Oral dosing with EPZ015666 demonstrated dose-dependent antitumor activity in multiple MCL xenograft models. EPZ015666 represents a validated chemical probe for further study of PRMT5 biology and arginine methylation in cancer and other diseases.

How to Use:

In vitro: EPZ015666 was used at 5 μM final concentration in various in vitro assays.

In vivo: EPZ015666 was dosed to MCL (Z-138, and Maver-1) xenograft animal models orally at 200 mg/Kg once per day.

Reference:

1. Chan-Penebre E, et al. A selective inhibitor of PRMT5 with in vivo and in vitro potency in MCL models. (2015) Nat Chem Biol. In press.