

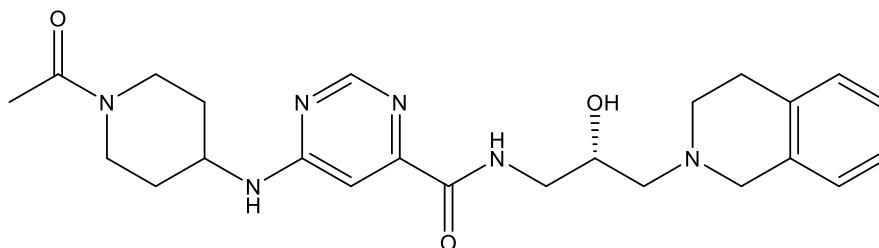
Catalog # 10-4028

GSK3326595

CAS# 1616392-22-3

6-[(1-Acetylpiperidine-4-yl)amino]-N-[(2S)-3-(3,4-dihydro-1H-isoquinolin-2-yl)-2-hydroxypropyl]pyrimidine-4-carboxamide;
EPZ015938

Lot # FBS2038



GSK3326595 is a potent ($IC_{50} = 6.2\text{nM}$), selective (>4000-fold over 20 other methyltransferases), SAM uncompetitive, peptide competitive inhibitor of PRMT5.1 PRMT5 inhibition activated the p53 pathway *via* induction of alternative splicing of MDM4 leading to a potent anti-proliferative response both *in vitro* and *in vivo*. Combination therapy with palbociclib (CDK4/6 inhibitor, Focus Cat.# 10-4760) and GSK3326595 lead to increased efficacy of palbociclib in treating native and resistant models of melanoma *via* regulation of the PRMT5-MDM4 axis.² Currently in clinical Trials.³

- 1) Gerhart *et al.* (2018), *Activation of the p53-MDM4 regulatory axis defines the anti-tumor response to PRMT5 inhibition through its role in regulating cellular splicing*; *Sci. Rep.* **8** 9711
- 2) AbuHammad *et al.* (2019), *Regulation of PRMT5-MDM4 axis is critical in the response to CDK4/6 inhibitors in melanoma*; *Proc. Natl. Acad. Sci. USA* **116** 179909
- 3) NCT02783300

PHYSICAL DATA

Molecular Weight:	452.56
Molecular Formula:	C ₂₄ H ₃₂ N ₆ O ₃
Purity:	>98% HPLC
	NMR: (Conforms)
Solubility:	Soluble in DMSO (20 mg/ml)
Physical Description:	Off-white solid
Storage and Stability:	Store as supplied at -20°C for up to 1 year from the date of purchase. Store solutions at -20°C for up to 1 month.

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