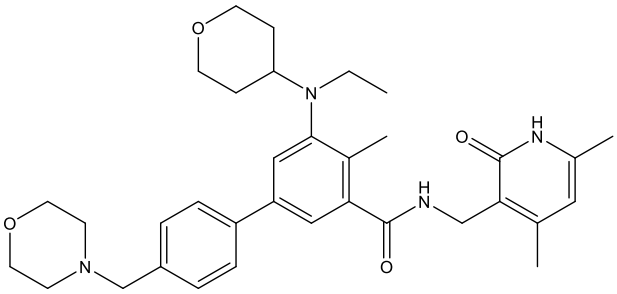
Catalog # 10-4032
Tazemetostat

CAS# 1403254-99-8

N-((4,6-Dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-5-(ethyl(tetrahydro-2H-pyran-4-yl)amino)-4-methyl-4'-(morpholinomethyl)-[1,1'-biphenyl]-3-carboxamide; EPZ-6438

Lot # X109182



Tazemetostat is a potent (Ki = 2.5nM wild type human PRC2-containing) and selective SAM-competitive inhibitor of the lysine methyltransferase EZH2.[1] Tazemetostat displayed strong antiproliferative effects against SMARCB1-deleted malignant rhabdoid tumor (MRT) cell lines *in vitro*. This antitumor activity was also observed in SMARTCB1 mutant mouse xenografts. It displayed potent antitumor activity in various cancer models including non-Hodgkins lymphoma[2], pediatric glioma[3], small-cell carcinoma of the ovary[4], and synovial sarcomas[5]. Tazemetostat has also been shown to control inflammatory genes by modulating IRF1, IRF8, and STAT1 levels suggesting therapeutic potential for the treatment of neuroinflammatory diseases associated with microglial activation.[6]

1) Knutson *et al.* (2013), *Durable tumor regression in genetically altered malignant rhabdoid tumors by inhibition of methyltransferase EZH2;* Proc. Natl. Acad. Sci. USA **110** 7922
2) Knutson *et al.* (2014), *Selective inhibition of EZH2 by EPZ-6438 leads to potent antitumor activity in EZH2-mutant non-Hodgkin lymphoma;* Mol.Cancer Ther. **13** 842
3) Mohammad *et al.* (2017), *EZH2 is a potential therapeutic target for H3K27M-mutant pediatric gliomas;* Nat. Med. **23** 483
4) Chan-Penebre *et al.* (2017), *Selective killing of SMARCA2- and SMARCA4-deficient Small Cell Carcinoma of the Ovary, Hypercalcemic Type Cells by Inhibition of EZH2: In Vitro and In Vivo Preclinical Models;* Mol. Cancer Ther. **16** 850
5) Kawano *et al.* (2016), *Preclinical Evidence of Anti-Tumor Activity by EZH2 Inhibition in Human Models of Synovial Sarcoma;* PLoS One **11** e0158888
6) Arifuzzaman *et al.* (2017), *Selective inhibition of EZH2 by a small molecule inhibitor regulates microglial gene expression essential for inflammation;* Biochem. Pharmacol. **137** 61

PHYSICAL DATA

Molecular Weight:	572.75
Molecular Formula:	$C_{34}H_{44}N_4O_4$
Purity:	>98% HPLC
	NMR: (Conforms)
Solubility:	Soluble in DMSO (>25 mg/ml)
Physical Description:	Off-white solid
Storage and Stability:	Store as supplied at -20ºC for up to 1 year from the date of purchase. Store solutions at -20ºC for up to 1 month.

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