

Product Data Sheet

Product Name: EPZ011989

Cat. No.: GC19141

Chemical Properties

Cas. No. 1598383-40-4

SMILES O=C(NCC1=C(C)C=C(C)NC1=O)C2=CC(C#CCN3CCOCC3)=CC(N(CC)[C@H]4CC[C@H](N(CCOC)C)CC4)=C2C

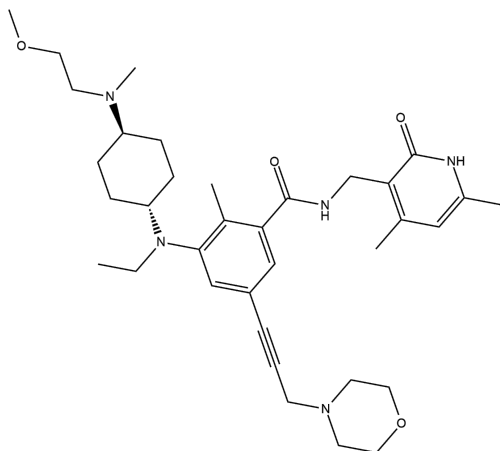
Formula $C_{35}H_{51}N_5O_4$ M.Wt 605.81

Solubility DMSO : ≥ 33 mg/mL (54.47 mM) Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Background

EPZ011989 is a potent, selective orally bioavailable EZH2 inhibitor with K_i 3000-fold selectivity over

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other HMTase. IC₅₀ value: 15-fold selectivity over EZH1 and >3000-fold selectivity relative to the K_i of 20 other histone methyltransferases (HMTs) tested. EPZ011989 also exhibits metabolic stability. Furthermore, EPZ011989 reduces cellular H3K27 methylation in the Y641F, mutant-bearing human lymphoma cell line, WSU-DLCL2, with an IC₅₀ below 100 nM. This functional response translates to activity in a long-term proliferation assay where EPZ011989 demonstrates an average lowest cytotoxic concentration (LCC) in WSU-DLCL2 cells of 208 nM. In vivo: The LCC parameter, when corrected for plasma protein-binding, predicts an efficacious plasma level in mouse for EPZ011989 of 158 ng/mL. The pharmacokinetics in SCID mice following oral administration of 125, 250, 500, and 1000 mg/kg indicated that the 1000 mg/kg dose provided coverage over the LCC for 24 h, while the 250 and 500 mg/kg doses provided coverage over this value for approximately 8 h. EPZ011989 demonstrates significant tumor growth inhibition in a mouse xenograft model of human B cell lymphoma.

References:

[1]. Campbell JE, et al. EPZ011989, A Potent, Orally-Available EZH2 Inhibitor with Robust in Vivo Activity. ACS Med Chem Lett. 2015 Mar 4;6(5):491-495.

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