

## Product Data Sheet

Product Name: UNC 0646

Cat. No.: GC16518

### Chemical Properties

Cas. No. 1320288-17-2

Chemical Name N-(1-cyclohexylpiperidin-4-yl)-6-methoxy-7-(3-piperidin-1-ylpropoxy)-2-(4-propan-2-yl-1,4-diazepan-1-yl)quinazolin-4-amine

SMILES CC(C)N1CCCN(CCC1)C2=NC3=CC(=C(C=C3C(=N2)NC4CCN(CC4)C5CCCCC5)OC)OC  
CCN6CCCCC6

Formula  $C_{36}H_{59}N_7O_2$

M.Wt 621.9

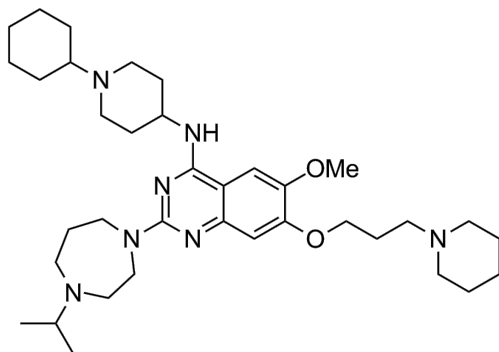
Solubility  $\geq 24.1$  mg/mL in DMSO with gentle warming,  $\geq 87$  mg/mL in EtOH

Storage Store at 4°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

IC50: 6 nm (G9a IC50); 26 nm (Cellular IC50); 3.3  $\mu$ M (Cell toxicity EC50)

Histone-lysine N-methyltransferase, H3 lysine-9 specific 3, also known as euchromatic histone-lysine N-methyltransferase 2 (EHMT2) and G9a, is a histone methyltransferase that in humans is encoded by the EHMT2 gene. Protein lysinemethyltransferase G9a plays key roles in the transcriptional

**Caution: Product has not been fully validated for medical applications. For research use only.**

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repression of a variety of genes via dimethylation of lysine 9 on histoneH3 (H3K9me2) of chromatin as well as dimethylation of nonhistone proteins including tumor suppressor p53.

In vitro: UNC0646 is reported to be a potent and selective inhibitor of the homologous protein lysine methyltransferases, G9a and GLP (IC<sub>50</sub> values are 6 nM and 15 nM for G9a and GLP, respectively). UNC0646 also potently blocks G9a/GLP methyltransferase activity in cells (IC<sub>50</sub> = 10 nM in MCF7 cells) and exhibits low cellular toxicity (EC<sub>50</sub> = 4.7  $\mu$ M in MCF7 cells). UNC0646 is selective for G9a/GLP over a range of other protein lysine methyltransferases and protein arginine methyltransferases [1].

In vivo: The authors previously discovered potent and selective G9a/GLP inhibitors including the cellular chemical probe UNC0638, which displays an excellent separation of functional potency and cell toxicity. However, this inhibitor is not suitable for animal studies due to its poor pharmacokinetic (PK) properties. In this study, the authors report the discovery of the first G9a and GLP in vivo chemical probe UNC0642, which not only maintains high in vitro and cellular potency, low cell toxicity, and excellent selectivity, but also displays improved in vivo PK properties, making it suitable for animal studies [2].

### References:

- [1] Liu F, Barsyte-Lovejoy D, Allali-Hassani A, He Y, Herold JM, Chen X, Yates CM, Frye SV, Brown PJ, Huang J, Vedadi M, Arrowsmith CH, Jin J. Optimization of cellular activity of G9a inhibitors 7-aminoalkoxy-quinazolines. *J Med Chem*. 2011;54(17):6139-50.
- [2] Liu F, Barsyte-Lovejoy D, Li F, Xiong Y, Korboukh V, Huang XP, Allali-Hassani A, Janzen WP, Roth BL, Frye SV, Arrowsmith CH, Brown PJ, Vedadi M, Jin J. Discovery of an in vivo chemical probe of the lysine methyltransferases G9a and GLP. *J Med Chem*. 2013;56(21):8931-42.

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