

Product Data Sheet

Product Name: GSK J4 free base

Cat. No.: GC12997

Chemical Properties

Cas. No. 1373423-53-0

Chemical Name ethyl 3-((6-(4,5-dihydro-1H-benzo[d]azepin-3(2H)-yl)-2-(pyridin-2-yl)pyrimidin-4-yl)amino)propanoate

SMILES CCOC(CCNC1=CC(N2CCC3=CC=CC=C3CC2)=NC(C4=CC=CC=N4)=N1)=O

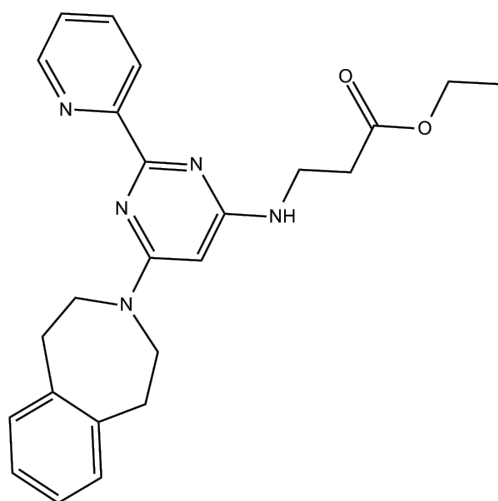
Formula $C_{24}H_{27}N_5O_2$ M.Wt 417.46

Solubility <41.75mg/ml in DMSO; <41.75mg/ml in ethanol 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

GSK-J4 is a potent dual inhibitor of H3K27me3/me2-demethylases JMJD3/KDM6B and UTX/KDM6A with IC50s of 8.6 and 6.6 μM, respectively. GSK-J4 inhibits LPS-induced TNF-α production in human primary macrophages with an IC50 of 9 μM. GSK J4 is a cell permeable prodrug of GSK-J1[1][2][3].

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

GSK-J4 has cellular activity in Flag-JMJD3-transfected HeLa cells, in which GSK-J4 prevents the JMJD3-induced loss of nuclear H3K27me3 immunostaining. Administration of GSK-J4 increases total nuclear H3K27me3 levels in untransfected cells. GSK-J4 significantly reduces the expression of 16 of 34 LPS-driven cytokines, including tumour-necrosis factor- α (TNF- α)[1]. GSK-J4 (5 μ M; 48 hours) causes a more than 3-fold increase in mouse podocyte H3K27me3 content. H3K27me3 levels in cultured podocytes, GSK-J4 reduces Jagged-1 mRNA and Jagged-1 protein levels. Correspondingly, when exposed podocytes to the inducer of dedifferentiation TGF- β 1, pretreatment with GSK-J4 prevents both the increase in intracellular N1-ICD levels and the increase in α -SMA and the decrease in podocin mRNA levels[2]. GSK-J4 (10, 25 nM) acts upon DCs promoting the differentiation of Treg cells, improving Treg stability and suppressive capacities, without affecting the differentiation of Th1 and Th17 cells[3]. GSK-J4 inhibits JMJD3 expression that is induced by TGF- β 1[4]. GSK-J4 inhibits H3K4 demethylation at Xist, Nodal, and HoxC13 in female embryonic stem cells[5].

GSK-J4 Hydrochloride (10 mg/kg; i.p.; thrice-weekly for 10 weeks) attenuates the development of kidney disease in diabetic mice[2]. GSK-J4 (0.5 mg/kg, i.p.) significantly reduces the severity and delays the onset of the disease of the mouse model of experimental autoimmune encephalomyelitis[3].

References:

- [1]. Kruidenier L, et al. A selective jumonji H3K27 demethylase inhibitor modulates the proinflammatory macrophage response. *Nature*. 2012 Aug 16;488(7411):404-8.
- [2]. Majumder S, et al. Shifts in podocyte histone H3K27me3 regulate mouse and human glomerular disease. *J Clin Invest*. 2018 Jan 2;128(1):483-499.
- [3]. Donas C, et al. The histone demethylase inhibitor GSK-J4 limits inflammation through the induction of a tolerogenic phenotype on DCs. *J Autoimmun*. 2016 Dec;75:105-117.
- [4]. Yapp C, et al. H3K27me3 demethylases regulate in vitro chondrogenesis and chondrocyte activity in osteoarthritis. *Arthritis Res Ther*. 2016 Jul 7;18(1):158
- [5]. Kamikawa YF, et al. Histone demethylation maintains Prdm14 and Tsix expression and represses xist in embryonic stem cells. *PLoS One*. 2015 May 20;10(5):e0125626
- [6]. Heinemann B, et al. Inhibition of demethylases by GSK-J1/J4. *Nature*. 2014 Oct 2;514(7520):E1-2

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA