

Product Data Sheet

Product Name: LY2409881

Cat. No.: GC10093

Chemical Properties

Cas. No. 946518-60-1

Chemical Name 2-(5-chloro-2-((3-(4-methylpiperazin-1-yl)propyl)amino)pyrimidin-4-yl)-N-cyclopropylbenzo[b]thiophene-4-carboxamide

SMILES C1C=CN=C(NCCCN2CCN(C)CC2)N=C1C3=CC4=C(S3)C=CC=C4C(NC5CC5)=O

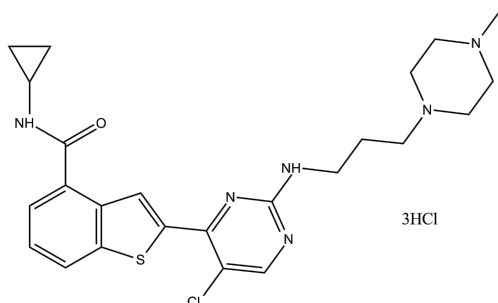
Formula $C_{24}H_{32}Cl_4N_6OS$ M.Wt 594.43

Solubility $\geq 59.4\text{mg/mL}$ in DMSO with ultrasonic 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



Protocol

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

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Cell experiment: OCI-Ly1, OCI-Ly7, and Su-DHL4 are GCB DLBCL cell lines; OCI-Ly3, OCI-Ly10, HBL1, and Su-DHL2 are ABC DLBCL lines. These cell lines are grown in Iscove Modified Dulbecco Medium with 10% FCS. Fresh medium is added every 2 to 3 days, and the cells are kept at a cell concentration of 0.1 to 1×10^6 /mL. Cytotoxicity is evaluated using the CellTiter-Glo Reagent. Experiments are carried out in 96-well plates, with each treatment in triplicate. Samples are taken at typically 24, 48, and 72 hours after treatment. Cytotoxicity is expressed by the decreasing percentage of live cells in each treatment (LY2409881; 0.01, 0.1, 1 and 10 μ M) relative to the untreated control from the same experiment, as a function of time. IC₅₀ for each cell line is calculated using the CalcuSyn Version 2.0 software[1].

Animal experiment: Mice[1] Mouse experiments are carried out. Five- to 7-week-old SCID beige mice are injected with 107 Ly10 cells mixed in Matrigel in the posterior flank subcutaneously. When the tumors approach 150 mm³, the mice are divided into four groups of 8 mice: (i) control group, which receive 5% dextrose in water; (ii) LY2409881 at 50 mg/kg in D5W; (iii) LY2409881 at 100 mg/kg in D5W; and (iv) LY2409881 at 200 mg/kg in D5W. LY2409881 or D5W is administered intraperitoneally on day 1 and 4 of every week for 4 weeks. The data are expressed as average tumor volume (mm³) per group as a function of time. Tumor volume is calculated.

References:

[1]. Deng C, et al. The novel IKK2 inhibitor LY2409881 potently synergizes with histone deacetylase inhibitors in preclinical models of lymphoma through the downregulation of NF- κ B. Clin Cancer Res. 2015 Jan 1;21(1):134-45.

Background

LY2409881 is a potent and selective inhibitor of IKK2 with IC₅₀ value of 30 nM [1].

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I κ B kinase β (IKK2) is an enzyme that serves as a subunit of I κ B kinase, which is involved in the cytokine-activated immune responses. IKK2 activates nuclear factor kappa-B kinase (NF- κ B).

LY2409881 is a selective IKK2 inhibitor and exhibited >10-fold selectivity over other common kinases and IKK1. In the ovarian cancer cell line SKOV3, LY2409881 showed moderate cytotoxicity. While coadministration of LY2409881 and TNF α significantly induced cells death, which suggested LY2409881 inhibited NF- κ B mediated antiapoptotic signals in a TNF α -dependent way. In the DLBCL cell line LY10, LY2409881 (10 μ M) inhibited TNF α -dependent phosphorylation of I κ B. In the DLBCL cell line SUDHL2, LY2409881 (10 μ M) inhibited the nuclear signals of p50 and NF- κ B. Also, LY2409881 induced apoptosis in a concentration-dependent way [1].

In SCID-beige mice bearing LY10 cell-derived tumors, LY2409881 (50, 100 and 200 mg/kg) significantly inhibited tumor growth [1].

Reference:

[1]. Deng C, Lipstein M, Rodriguez R, et al. The novel IKK2 inhibitor LY2409881 potently synergizes with histone deacetylase inhibitors in preclinical models of lymphoma through the downregulation of NF- κ B. Clin Cancer Res, 2015, 21(1): 134-145.

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