

Product Data Sheet

Product Name: LY2835219 free base

Cat. No.: GC11823

Chemical Properties

Cas. No. 1231929-97-7

Chemical Name N-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoro-4-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)pyrimidin-2-amine

SMILES CCN1CCN(CC2=CN=C(NC3=NC=C(F)C(C4=CC5=C(N=C(C)N5C(C)C)C(F)=C4)=N3)C=C2)CC1

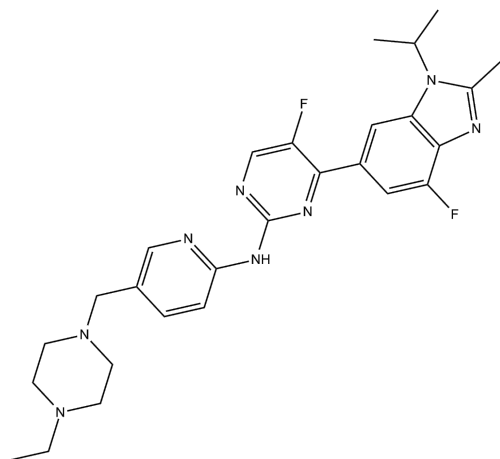
Formula $C_{27}H_{32}F_2N_8$ M.Wt 506.59

Solubility ≥ 4.83 mg/mL in DMSO with ultrasonic and warming, ≥ 6.34 mg/mL in EtOH with gentle warming
Storage 4°C , protect from light

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

Cell experiment [1]:

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

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Cell lines Colo-205 colorectal cells

Preparation Method Colo-205 colorectal cells treated with LY2835219 free base (0.001-10 μ M) for 24h.

Reaction
Conditions LY2835219 free base: 0.001-10 μ M; 24h

Applications LY2835219 free base treated with Colo-205 colorectal cells showed a concentration-dependent inhibition of p-Rb and a corresponding arrest of cells in G1 (2 N DNA content), resulting in a decreased number of cells due to inhibition of proliferation.

Animal experiment [2]:

Animal models Colo-205 human xenograft tumor model

Preparation Method LY2835219 free base was formulated in 1 % hydroxyethyl cellulose + 0.1 % antifoam in 25mM PBS pH 2 and administered orally by gavage (final volume 0.2 mL) at the indicated dose and schedule.

Dosage form LY2835219 free base (50mg/kg; po; 56d)

Applications LY2835219 free base is effective and well tolerated when administered up to 56 days in Colo-205 human xenograft tumor mice without significant loss of body weight or tumor outgrowth.

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References:

[1]. Gelbert LM, Cai S, Lin X, Sanchez-Martinez C, Del Prado M, Lallena MJ, Torres R, Ajamie RT, Wishart GN, Flack RS, Neubauer BL, Young J, Chan EM, Iversen P, Cronier D, Kreklau E, de Dios A. Preclinical characterization of the CDK4/6 inhibitor LY2835219: in-vivo cell cycle-dependent/independent anti-tumor activities alone/in combination with gemcitabine. Invest New Drugs. 2014 Oct;32(5):825-37.

Background

LY2835219 free base is a potent and selective inhibitor of CDK4 and CDK6 with IC₅₀ of 2nM and 10nM in cell-free assays, respectively^[1].

LY2835219 free base (0.001-10μM; 24h) inhibited p-Rb in a concentration-dependent manner, resulting in cell arrest in the G1 phase (2 N DNA content) and a decrease in cell number due to inhibition of proliferation. LY2835219 free base inhibits CDK4 and CDK6 with low nanomolar potency, inhibits Rb phosphorylation resulting in a G1 arrest and inhibition of proliferation, and its activity is specific for Rb-proficient cells^[2]. LY2835219 free base (0.1, 0.2 and 0.4μM; 24h) potentiated the cytotoxicity of conventional chemotherapeutic agents in ABCB1 and ABCG2-overexpressing cells^[3].

LY2835219 free base (50mg/kg; po; 56d) was effective and well tolerated in mice bearing Colo-205 xenograft tumors. After administration for up to 56days, there was no significant weight loss in mice and no significant tumor growth^[2]. LY2835219 free base (45mg/kg; po; 14d) combined with RAD001 had a synergistic anti-tumor effect on HNSCC xenograft tumors^[4].

References:

- [1].Corona SP, Generali D. Abemaciclib: a CDK4/6 inhibitor for the treatment of HR+/HER2-advanced breast cancer. Drug Des Devel Ther. 2018 Feb 16;12:321-330.
- [2]. Gelbert LM, Cai S, Lin X, Sanchez-Martinez C, Del Prado M, Lallena MJ, Torres R, Ajamie RT, Wishart GN, Flack RS, Neubauer BL, Young J, Chan EM, Iversen P, Cronier D, Kreklau E, de Dios A. Preclinical characterization of the CDK4/6 inhibitor LY2835219: in-vivo cell cycle-dependent/independent anti-tumor activities alone/in combination with gemcitabine. Invest New Drugs. 2014 Oct;32(5):825-37.
- [3]Wu T, Chen Z, To KKW, Fang X, Wang F, Cheng B, Fu L. Effect of abemaciclib (LY2835219) on

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enhancement of chemotherapeutic agents in ABCB1 and ABCG2 overexpressing cells in vitro and in vivo. Biochem Pharmacol. 2017 Jan 15;124:29-42.

[4]. Ku BM, Yi SY, Koh J, Bae YH, Sun JM, Lee SH, Ahn JS, Park K, Ahn MJ. The CDK4/6 inhibitor LY2835219 has potent activity in combination with mTOR inhibitor in head and neck squamous cell carcinoma. Oncotarget. 2016 Mar 22;7(12):14803-13.

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