Chemical Properties

Product Name: LY2784544
Cas No.: 1229236-86-5
M.Wt: 469.94
Formula: C23H25ClFN7O

Chemical Name: 3-[(4-chloro-2-fluorophenyl)methyl]-2-methyl-N-(5-methyl-1H-pyrazol-3-yl)-8-(morpholin-4-ylmethyl)imidazo[1,2-b]pyridazin-6-amine
Canonical SMILES: CC1=CC(=NN1)NC2=NN3C(=C(N=C3C(=C2)CN4CCOC4)C)CC5=C(C=C(C=C5)Cl)F

Solubility: $\geq 23.5$ mg/mL in DMSO, $\geq 5.65$ mg/mL in EtOH with ultrasonic and warming, insoluble in H2O

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.

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

Biological Activity

Targets: Chromatin/Epigenetics
Pathways: JAK

Description:

LY2784544 is a potent, selective inhibitor of JAK2 with IC50 value of 3 nM.[1] Janus kinase 2 (JAK2) belongs to the Janus kinase family and is a member of the type II cytokine receptor family. It is a non-receptor tyrosine kinase. The JAK2 mutation (V617F) within the autoinhibitory pseudokinase domain results in a gain-of-function activation of JAK2. The
JAK2V617F mutant results in subsequent phosphorylation of signal transducer and activator of transcription 5 (STAT5). Then, STAT5 regulates the transcription of genes associated with cell growth, death and differentiation. The JAK2V617F mutant is oncogenic in cells, and sufficient for generating the myeloproliferative neoplasms (MPN) phenotypes in murine models. Mutant JAK2 kinase is an attractive therapeutic target for the therapy of MPNs. To selectively inhibit JAK2V617F but minimizing inhibition of wild-type JAK2 would be an optimal treatment approach. LY2784544 is a potent and ATP-competitive inhibitor of JAK2 tyrosine kinase. LY2784544 has 8- and 16-fold selectivity for JAK2 than JAK1 and JAK3, respectively. LY2784544 more effective on inhibiting the phosphorylation of STAT5 in Ba/F3-TEL-JAK2 cells than in Ba/F3-TEL- JAK3 and – JAK1 cells with IC50 of 0.191 (JAK2), 2.904 (JAK1) and 4.744 nM (JAK3). LY2784544 significantly inhibited STAT5 phosphorylation at a concentration range from 50 nM-20 nM in Ba/F3 cells expressing JAK2V617F. On the other hand, LY2784544 showed minimal inhibition of STAT5 phosphorylation at 50 and 200 nM concentrations in IL-3-stimulated Ba/F3 cells which express wild-type JAK2. LY2784544 significantly inhibited the cell proliferation of JAK2V617F-expressing cells with IC50 = 55 nM. In JAK2V617F-expressing cells, LY2784544 induced apoptosis with EC50 ± s.d.of 113 ± 0.023 nM measured by Caspase3/7-glo assays. LY2784544 with a TED50 (threshold effective Dose 50) of 12.7 mg/kg, potently inhibits STAT5 phosphorylation in SCID mice bearing Ba/F3-JAK2V617F-GFP. In mouse hematologic disease model, LY2784544 also dose-dependently reduces Ba/F3-JAK2V617F-GFP tumor burden.

Reference:

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Short-term storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.