Product Data Sheet

Chemical Properties

Product Name: PF-03814735
Cas No.: 942487-16-3
M.Wt: 474.48
Formula: \text{C}23\text{H}25\text{F3N6O2}

Chemical Name:
Canonical SMILES: \text{CC(=O)NCC(=O)N1C2CCC1C3=C2C=CC(=C3)NC4=NC=C(=N4)NC5CC C5)C(F)(F)F}

Solubility: Soluble in DMSO
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: Aurora Kinase
Description:

PF-03814735 is a potent, orally bioavailable, reversible inhibitor of both Aurora1 and Aurora2 kinases with IC50 values of 0.8nM and 5nM, respectively [1]. PF-03814735 is an ATP competitive inhibitor of Aurora kinases. It also shows inhibition of other
protein kinases at 100nM, such as Flt1, FAK, TrkA, Met, and FGFR1. The immunofluorescence imaging analysis shows PF-03814735 can inhibit the phosphorylation of Aurora1, Aurora 2 as well as histone H3 in MDA-MB-231 cells. This inhibition is rapid and reversible. The inhibition of phosphorylated histone H3 also occurs in athymic mice bearing HCT-116 xenografts. PF-03814735 induces the formation of polyploid cells and multinucleated cells due to the block in cytokinesis secondary. Moreover, PF-03814735 treatment results in a reduction of cell proliferation in vitro (such as HL-60, A549, and H125) and a inhibition of tumor growth in vivo (human xenograft mouse models, such as A2780 ovarian carcinoma and HCT-116) [1].

Reference:

### Protocol

#### Cell experiment:

| Cell lines | MDA-MB-231 cells, various tumor types (HCT-116, HL-60, A549, and H125) as well as tumor cell lines of rat (C6), mouse (L1210), and dog (MDCK) origin. |
| Preparation method | The solubility of this compound in DMSO is > 10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37°C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months. |
| Reacting conditions | In MDA-MB-231 cells, PF-03814735 markedly reduced levels of Aurora1 phosphorylated on Thr 232 and the phosphorylation of histone H3 on Ser10 with IC50 values of 20 nmol/L and 50 nmol/L. In various tumor cell lines, PF-03814735 resulted in a reduction in cell number with IC50 values ranging from 42 to 150 nmol/L. PF-03814735 at 300 nmol/L produced near-complete inhibition of cell proliferation. |

#### Animal experiment [3]:

| Animal models | Athymic mice bearing s.c. HCT-116 human colorectal cancer xenografts |
| Dosage form | 10, 20, and 30 mg/kg; oral gavage for 10 days |
Applications

In athymic mice bearing s.c. HCT-116 human colorectal cancer xenografts, PF-03814735 (≥20 mg/kg) resulted in statistically significant and dose-dependent tumor growth inhibition of ≥50% relative to vehicle-treated mice. The tumor growth inhibition was associated with a reduction in phosphorylated histone H3 levels of ≥50% for approximately 5 hours each day for 10 days.

Other notes

Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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.