Product Data Sheet

Product Name: PF-03814735
Cat. No.: GC18074

Chemical Properties

Cas. No.	942487-16-3		
SMILES	CC(=O)NCC(=O)N1C2CCC1C3=C2C=CC(=C3)NC4=NC=C(C(=N4)NC5CCC5)C(F)(F)F		
Formula	$C_{23}H_{25}F_3N_6O_2$	M.Wt	474.48
Solubility	DMF: 20 mg/ml,DMSO: 16 mg/ml,Ethanol: 20 mg/ml,Ethanol:PBS (pH 7.2) (1:9): 0.10 mg/ml	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.		

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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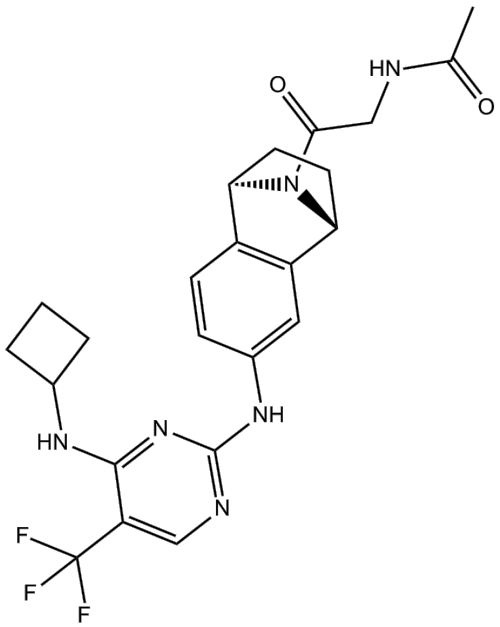
Structure



Protocol

Cell experiment [1]:

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 condition	1-1000 nM; 4, 8, 12, 24, and 48 h

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Applications	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 [1]:

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
Application	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.

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References:

[1] Jani JP, Arcari J, Bernardo V, Bhattacharya SK, Briere D, Cohen BD, Coleman K, Christensen JG, Emerson EO, Jakowski A, Hook K, Los G, Moyer JD, Pruimboom-Brees I, Pustilnik L, Rossi AM, Steyn SJ, Su C, Tsaparikos K, Wishka D, Yoon K, Jakubczak JL. PF-03814735, an orally bioavailable small molecule aurora kinase inhibitor for cancer therapy. Mol Cancer Ther. 2010 Apr;9(4):883-94.

Background

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].

References:
[1] Jani JP, Arcari J, Bernardo V, Bhattacharya SK, Briere D, Cohen BD, Coleman K, Christensen JG, Emerson EO, Jakowski A, Hook K, Los G, Moyer JD, Pruimboom-Brees I, Pustilnik L, Rossi AM, Steyn SJ, Su C, Tsaparikos K, Wishka D, Yoon K, Jakubczak JL. PF-03814735, an orally bioavailable small molecule aurora kinase inhibitor for cancer therapy. Mol Cancer Ther. 2010 Apr;9(4):883-94.