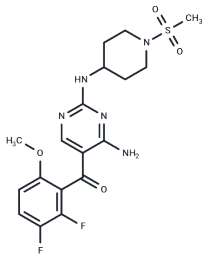
Data Sheet (Cat.No.T6312)

TargetMol

R547

Chemical Properties



CAS No. : 741713-40-6

Formula: C18H21F2N5O4S

Molecular Weight: 441.45

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	R547 (Ro 4584820) is a potent ATP-competitive inhibitor of CDK1/2/4 with Ki of 2 nM/3 nM/1 nM. It is less potent to CDK7 and GSK3α/β, while inactive to other kinases. Phase 1.
Targets(IC50)	Apoptosis,CDK,GSK-3,PKA
In vitro	R547 identified as a diaminopyrimidine compound, which is a potent and selective ATP-competitive CDK inhibitor. R547 effectively inhibits CDK1/cyclinB, CDK2/cyclinE, and CDK4/cyclinD1(Ki=1-3 nM) and is inactive(Ki>5,000 nM) against a panel of >120 unrelated kinases. R547 effectively inhibits the proliferation of tumor cell lines independent of multidrug resistant status, histologic type, retinoblastoma protein, or p53 status, with IC50s <0.60 μM. R547 reduces phosphorylation of the cellular retinoblastoma protein at specific CDK phosphorylation sites at the same concentrations that induced cell cycle arrest, suggesting a potential pharmaco dynamics marker for clinical use. R547 inhibits the proliferation of tumor cell lines and is active in all 19 cell lines tested irrespective of tissue of origin, multidrug resistance (MDR), p53, or retinoblastoma status. [1] R547 possessing both 5-and 6-fluoro substitution culminated in an Inhibitor with low, single-digit nanomolar potency against the CDKs(Ki=0. 001,0.003,and 0.001 μM for CDK1,CDK2, and CDK4,respectively) and excellent cellular potency (IC50=0.08 μM,HCT116 cell line). [2]
In vivo	R547 administered with oral and i.v. dosing in multiple established human tumor significantly inhibits tumor activity(P < 0.01). R547 administered orally at dose of 40 mg/kg daily in colon, lung, breast, prostate, and melanoma human tumor xenograft models shows significant TGI (79-99%). R547 is equally efficacious (TGI, 61-95%) when dosed with 40 mg/kg i.v. once weekly. These doses of R547 are not toxic and did not result in body weight loss. R547 does not show signs of overt toxicity during the course of the 3-week study and any gross pathology at necropsies done at the end of the studies. [1] R547 inhibits tumor growth up to 95% in the HCT116 human colorectal tumor xenograft model in nude mice . R547 causes significant TGI in all of the models tested when dosed orally and i.v. at or below the maximum tolerated dose. R547 inhibits phosphorylation of retinoblastoma protein in tumors at the efficacious exposures in tumor xenograft models, providing a pharmacodynamic biomarker for clinical use. R547 reported here suggests that this is a promising molecule for evaluation in the treatment of solid tumors. [2]

Solubility Information

Solubility	Ethanol: < 1 mg/mL (insoluble or slightly soluble), H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 60 mg/mL (135.92 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2653 mL	11.3263 mL	22.6526 mL
5 mM	0.4531 mL	2.2653 mL	4.5305 mL
10 mM	0.2265 mL	1.1326 mL	2.2653 mL
50 mM	0.0453 mL	0.2265 mL	0.4531 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Rodriguez A , et al. Mol Cancer Ther, 2006, 5(11), 2644-2658.
Chu XJ, et al. J Med Chem, 2006, 49(22), 6549-6560.
Berkofsky-Fessler W, et al. Mol Cancer Ther, 2009, 8(9), 2517-2525.