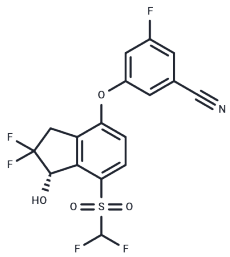
Data Sheet (Cat.No.T12675L)

PT2399

Chemical Properties



CAS No. : 1672662-14-4

Formula: C17H10F5NO4S

Molecular Weight: 419.32

Appearance: no data available

Storage: store at low temperature,store under nitrogen
Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	PT2399 is a first-in-class, orally available, small molecule inhibitor of HIF-2 that selectively disrupts the heterodimerization of HIF-2α with HIF-1β. PT2399 displays potent antitumor activity in vivo
Targets(IC50)	HIF/HIF Prolyl-Hydroxylase,HIF
In vitro	PT2399, a selective HIF-2 antagonist that was identified using a structure-based design approach. PT2399 dissociated HIF-2 (an obligatory heterodimer of HIF-2α-HIF-1β) in human ccRCC cells and suppressed tumorigenesis in 56% (10 out of 18) of such lines[1]. PT2399 inhibits HIF-2α (IC50: 6 nM). PT2399 represses various HIF target genes in 786-O VHL / ccRCC cells, does not suppress HIF-1α-specific targets such as BNIP3. PT2399 can cripple HIF-2α's ability to bind to Aryl hydrocarbon receptor nuclear translocator (ARNT). PT2399 (20 μM) induces off-target toxicity because it inhibits the proliferation of HIF-2α / 786-O cells and other cancer cell lines with undetectable HIF-2α. PT2399 (0.2-2 μM; 0-21 days) inhibits 786-O cells soft agar growth[2][3].
In vivo	PT2399) that directly inhibits HIF-2α causes tumour regression in preclinical mouse models of primary and metastatic pVHL-defective clear cell renal cell carcinoma in an on-target fashion[2].PT2399 inhibits tumor cell proliferation 3.5 fold in renal cell carcinoma (RCC) bearing mice.PT2399 directly inhibits HIF-2α causes tumor regression in preclinical models of primary and metastatic pVHL-defective ccRCC in an on-target fashion.PT2399 reduces tumor cell density and increases fibrosis in RCC bearing mice. PT2399 (100 mg/kg;oral gavage;every 12 hours) is more active than SU 11248 and inhibits tumor growth in several SU 11248-resistant tumors in RCC bearing mice [1][2].

Solubility Information

Solubility	DMSO: 200 mg/mL (476.96 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.3848 mL	11.9241 mL	23.8481 mL
5 mM	0.477 mL	2.3848 mL	4.7696 mL
10 mM	0.2385 mL	1.1924 mL	2.3848 mL
50 mM	0.0477 mL	0.2385 mL	0.477 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

Chen W, et al. Targeting renal cell carcinoma with a HIF-2 antagonist. Nature. 2016 Nov 3;539(7627):112-117.
Cho H, et al. On-Target Efficacy of a HIF2α Antagonist in Preclinical Kidney Cancer Models. Nature. Nature. 2016 Nov 3;539(7627):107-111.
Wehn PM, et al. Design and Activity of Specific Hypoxia-Inducible Factor-2α (HIF-2α) Inhibitors for the Treatment of Clear Cell Renal Cell Carcinoma: Discovery of Clinical Candidate (S)-3-((2,2-Difluoro-1-hydroxy-7-(methylsulfonyl)-2,3-dihydro-1 H-inden-4-yl)oxy)-5-fluorobenzonitrile (PT2385). J Med Chem. 2018 Nov 8;61(21):9691-9721.