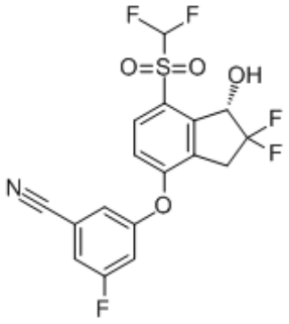
PT2399

Cat. No.:	HY-108697
CAS No.:	1672662-14-4
Molecular Formula:	$C_{17}H_{10}F_5NO_4S$
Molecular Weight:	419.32
Target:	HIF/HIF Prolyl-Hydroxylase
Pathway:	Metabolic Enzyme/Protease
Storage:	-20°C, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 200 mg/mL (476.96 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3848 mL	11.9241 mL	23.8481 mL
5 mM	0.4770 mL	2.3848 mL	4.7696 mL
10 mM	0.2385 mL	1.1924 mL	2.3848 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.67 mg/mL (3.98 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.67 mg/mL (3.98 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (3.98 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PT2399 is a potent and selective HIF-2α antagonist, which directly binds to HIF-2α PAS B domain with an IC_{50} of 6 nM. PT2399 displays potent antitumor activity in vivo[1][2][3].

IC_{50} & Target

IC50: 6 nM (HIF-2α)[3]

In Vitro

PT2399 (compound 10f) inhibits HIF-2α with an IC_{50} of 6 nM[3].
PT2399 can bind directly to the HIF-2α PAS B domain, and cripple HIF-2α's ability to bind to Aryl hydrocarbon receptor nuclear translocator (ARNT)[2].

PT2399 (20 μM) causes off-target toxicity because it inhibits the proliferation of HIF-2α −/− 786-O cells and other cancer cell lines with undetectable HIF-2α[2].
PT2399 (0.2–2 μM; 0-21 days) inhibits 786-O cells soft agar growth[2].
PT2399 represses various HIF target genes in 786-O VHL−/− ccRCC cells, does not suppress HIF-1α-specific targets such as BNIP3[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	786-O cells
Concentration:	0 μM, 0.2 μM, 2 μM
Incubation Time:	0-21 days
Result:	Inhibited 786-O cell soft agar growth at 0.2–2 μM.

In Vivo

PT2399 inhibits tumor cell proliferation 3.5 fold in renal cell carcinoma (RCC) bearing mice[1].
PT2399 reduces tumor cell density and increases fibrosis in RCC bearing mice[1].
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].
PT2399 directly inhibits HIF-2α causes tumor regression in preclinical models of primary and metastatic pVHL-defective ccRCC in an on-target fashion[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Mice with RCC tumorgraft[1]
Dosage:	100 mg/kg
Administration:	Oral gavage; every 12 hours
Result:	More active than SU 11248, and inhibited tumor growth in several SU 11248-resistant tumors.

CUSTOMER VALIDATION

- Biomed Pharmacother. 2021 May 29;140:111778.

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REFERENCES

[1]. Chen W, et al. Targeting renal cell carcinoma with a HIF-2 antagonist. Nature. 2016 Nov 3;539(7627):112-117.

[2]. 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.

[3]. 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.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA