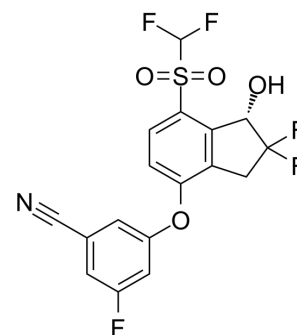


PT2399

Cat. No.:	HY-108697
CAS No.:	1672662-14-4
Molecular Formula:	C ₁₇ H ₁₀ F ₅ NO ₄ S
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 Concentration	Mass		
		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

- 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
- 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
- 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 IC₅₀ of 6 nM. PT2399 displays potent antitumor activity in vivo^{[1][2][3]}.

IC₅₀ & Target

IC₅₀: 6 nM (HIF-2α)^[3]

In Vitro

PT2399 (compound 10f) inhibits HIF-2α with an IC₅₀ 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-2 α $-/-$ 786-O cells and other cancer cell lines with undetectable HIF-2 α ^[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-1 α -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-2 α 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

- EMBO J. 2023 Sep 4;e113743.
- Biomed Pharmacother. 2021 May 29;140:111778.
- J Biol Eng. 2024 Jan 22;18(1):11.
- FASEB J. 2022 Jul;36(7):e22410.
- Hum Mol Genet. 2023 Jun 1;ddad091.

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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 HIF2 α 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-2 α (HIF-2 α) Inhibitors for the Treatment of Clear Cell Renal Cell Carcinoma: Discovery of Clinical

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