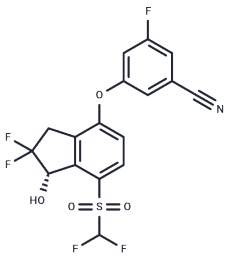
Data Sheet (Cat.No.T12675L)

TargetMol

PT2399

Chemical Properties



CAS No. : 1672662-14-4

Formula: C17H10F5NO4S

Molecular Weight: 419.32

Storage: Store at low temperature,Store under nitrogen
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	PT2399 is a potent, selective, orally available HIF-2α antagonist that directly binds to the PAS B domain of HIF-2α (IC_{50} = 6 nM). PT2399 exhibits antitumor activity. PT2399 specifically blocks the heterodimerization of HIF-2α and HIF-1β, thereby inhibiting the expression of downstream target genes such as VEGF and GLUT1, and exerts its antitumor effects.
Targets(IC50)	HIF/HIF Prolyl-Hydroxylase,HIF
In vitro	**Methods**: HEK293T cells were co-transfected with HIF-2α G323E and HIF-1β F446L expression plasmids. After 36 hours, cells were treated with PT2399 (10 μM) for 5 hours at 37 °C. Immunoprecipitation was performed using anti-FLAG beads (A2220-1ML, Sigma), followed by Western blot analysis. **Results**: HIF-2α G323E and HIF-1β F446L mutations maintained HIF-2 dimer stability against PT2399-induced dissociation. [1] **Methods**: RAW 264.7 macrophages were induced to M2 polarization with IL-4/IL-13 (10 ng/mL). Conditioned medium collected after 48 hours of treatment with PT2399 (0.1, 1, 10 μM) in CAFs cultured under 1% O_2 hypoxia was used for 48-hour treatment. RT-qPCR detected Arg1 mRNA levels as an M2 marker. **Results**: Hypoxic CAF-conditioned medium (CM) significantly enhanced IL-4/13-induced Arg1 expression (promoting M2 polarization). Following PT2399 treatment of CAFs, the pro-M2-polarizing effect of their CM was abolished. [2]
In vivo	**Methods**: Immunodeficient mice (NOD/SCID) were used to establish a xenograft tumor model. Following successful tumor implantation, oral gavage administration was performed (Sunitinib, 10 mg/kg; PT2399, 100 mg/kg) for 4 consecutive weeks. **Results**: In sensitive tumors, PT2399 significantly downregulated HIF-2 target gene expression and inhibited tumor cell proliferation and angiogenesis. [1] **Methods**: C57BL/6 mice were orthotopically inoculated with KPC cells in the pancreas. Following successful inoculation, oral administration of PT2399 (50 mg/kg) was administered twice daily, 5 days per week, for 3 weeks; Intraperitoneal injection of αCTLA4 + αPD1 (dual immune checkpoint blockade, DCB) every 4 days for 2 weeks, with monitoring up to 45 days. **Results**: The PT2399 + DCB combination therapy group achieved a 100% survival rate at 45 days, significantly higher than the control group and superior to the DCB monotherapy group. [2]

In vivo	**Methods**: Spinal disc degeneration (APD) model induced by needle puncture in SD rats. PT2399 (10 nmol/kg) administered via local injection through the puncture needle post-surgery; PT2399-PHBV/PP20 (containing equivalent PT2399) administered as a single injection. Animals euthanized at 4, 6, and 8 weeks for tissue collection. **Results**: In the APD+PT2399-PHBV and APD+PT2399-PP20 groups, histological scores showed a smaller increase and the height/width ratio exhibited a smaller decrease at 6 and 8 weeks, indicating a slowed degeneration process. [3]

Solubility Information

Solubility	DMSO: 262.5 mg/mL (626.01 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 5 mg/mL (11.92 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

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.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Chen W, et al. Targeting renal cell carcinoma with a HIF-2 antagonist. Nature. 2016 Nov 3;539(7627):112-117.
Garcia Garcia CJ, et al. Stromal HIF2 Regulates Immune Suppression in the Pancreatic Cancer Microenvironment. Gastroenterology. 2022 Jun;162(7):2018-2031.
Li Z, et al. Poly-3-hydroxybutyrate-co-3-hydroxyvalerate(PHBV)-Polyethylene glycol 20k(PEG20k) as a promising delivery system for PT2399 in the treatment of disc degeneration. J Biol Eng. 2024 Jan 22;18(1):11.

Tel:781-999-4286 E_mail:info@targetmol.com Address:34 Washington Street,Wellesley Hills,MA 02481