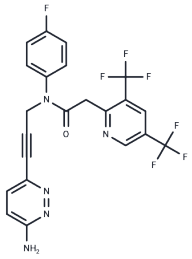
Data Sheet (Cat.No.T60187)

TargetMol

RP-6685

Chemical Properties



CAS No. : 2832047-80-8

Formula: C22H14F7N5O

Molecular Weight: 497.37

Storage: Keep away from direct sunlight
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	RP-6685, a highly potent and selective inhibitor of DNA polymerase theta (Polθ), manifests remarkable oral activity. With an IC 50 value of 5.8 nM in the PicoGreen assay, RP-6685 effectively hinders the enzymatic activity of Polθ. In addition, it demonstrates significant antitumor efficacy as observed in a mouse tumor xenograft model [1].
Targets(IC50)	DNA/RNA Synthesis
In vitro	RP-6685 demonstrates high potency, with an IC50 of 550 pM against the pol activity of full-length Polθ and no effect on ATPase activity [1]. In HEK293 LIG4 -/- cells, RP-6685 inhibits Polθ with an IC50 of 0.94 μM [1].
In vivo	Administering RP-6685 at a dosage of 80 mg/kg orally twice a day for 21 days demonstrated significant antitumor activity in BRCA2-deficient HCT116 mouse models. Despite inducing tumor regression within the first 8 days of treatment in BRCA2 -/- HCT116 models, it proved ineffective in BRCA2 +/+ HCT116 tumors. In another assessment using CD1 mice weighing 20-30 g, a single dose of either 2.5 mg/kg intravenously or orally was tested, yielding pharmacokinetic parameters of clearance (CL) at 36.8 mL/min/kg, a steady-state volume of distribution (V dss) at 1.1 L/kg, a half-life (t 1/2) of 0.4 hours, and a bioavailability (F) of 66%.

Solubility Information

Solubility	DMSO: 150 mg/mL (301.59 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+90% Corn Oil: 3.3 mg/mL (6.63 mM),Sonication is recommended. 10% DMSO+90% Saline: 10 mg/mL (20.11 mM),Suspension. *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	2.0106 mL	10.0529 mL	20.1058 mL
5 mM	0.4021 mL	2.0106 mL	4.0212 mL
10 mM	0.2011 mL	1.0053 mL	2.0106 mL
50 mM	0.0402 mL	0.2011 mL	0.4021 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

Bubenik M, et al. Identification of RP-6685, an Orally Bioavailable Compound that Inhibits the DNA Polymerase Activity of Polθ. J Med Chem. 2022 Sep 20.