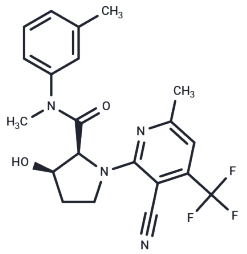
Data Sheet (Cat.No.T9275)

TargetMol

ART558

Chemical Properties



CAS No. : 2603528-97-6

Formula: C21H21F3N4O2

Molecular Weight: 418.41

Storage: 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	ART558 is a potent, selective, low molecular weight, allosteric DNA polymerase activity of Polθ inhibitor (IC50=7.9 nM). ART558 can be used for the research of cancer.
Targets(IC50)	DNA/RNA Synthesis
In vitro	ART558 (5μM; 0~72 hours; BRCA2wild-type or BRCA2/ cells) shows γH2AX accumulation in cells. ART558 (0~10 μM; 7 days; BRCA2wild-type or BRCA2/ cells) shows synthetic lethality and a combinatorial effect with the PARPi olaparib in previously described isogenic models of BRCA1-deficiency. ART558 inhibits the major Polθ mediated DNA repair process, Theta-Mediated End Joining, without targeting NonHomologous End Joining. ART558 elicits DNA damage and synthetic lethality in BRCA1- or BRCA2-mutant tumour cells and enhances the effects of a PARP inhibitor. ART558 increases biomarkers of single-stranded DNA and synthetic lethality in 53BP1-defective cells whilst the inhibition of DNA nucleases that promote end-resection reversed these effects, implicating these in the synthetic lethal mechanism-of-action. ART558 increases the residence time of YFP-tagged full-length Polθ at sites of laserinduced DNA damage[1].

Solubility Information

Solubility	DMSO: 45 mg/mL (107.55 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+90% Corn Oil: 4 mg/mL (9.56 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	2.390 mL	11.950 mL	23.900 mL
5 mM	0.478 mL	2.390 mL	4.780 mL
10 mM	0.239 mL	1.195 mL	2.390 mL
50 mM	0.0478 mL	0.239 mL	0.478 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

Zatreanu D, et al. Polθ inhibitors elicit BRCA-gene synthetic lethality and target PARP inhibitor resistance. Nat Commun. 2021 Jun 17;12(1):3636.
Rodriguez-Berriguete G, et al. Small-Molecule Polθ Inhibitors Provide Safe and Effective Tumor Radiosensitization in Preclinical Models. Clin Cancer Res. 2023 Apr 14;29(8):1631-1642.