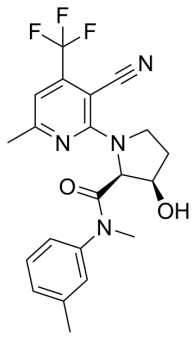
ART558

Cat. No.:	HY-141520
CAS No.:	2603528-97-6
Molecular Formula:	$C_{21}H_{21}F_3N_4O_2$
Molecular Weight:	418.41
Target:	DNA/RNA Synthesis
Pathway:	Cell Cycle/DNA Damage
Storage:	4°C, sealed storage, away from moisture and light * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 170 mg/mL (406.30 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3900 mL	11.9500 mL	23.9000 mL
	5 mM	0.4780 mL	2.3900 mL	4.7800 mL
	10 mM	0.2390 mL	1.1950 mL	2.3900 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5 mg/mL (11.95 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 4.25 mg/mL (10.16 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

ART558 is a nanomolar potent, selective, low molecular weight, allosteric DNA polymerase activity of Polθ inhibitor (IC_{50}=7.9 nM). ART558 can be used for the research of cancer[1].

IC_{50} & Target

IC50: 7.9 nM (Polθ)[1]

In Vitro

ART558 (0~10 μM; 7 days; $BRCA2^{wild\text{-}type}$ or $BRCA2^{-/-}$ cells) shows synthetic lethality and a combinatorial effect with the PARPi olaparib in previously described isogenic models of BRCA1-deficiency[1].
ART558 (5μM; 0~72 hours; $BRCA2^{wild\text{-}type}$ or $BRCA2^{-/-}$ cells) shows γH2AX accumulation in cells[1].
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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	BRCA2$^{wild\text{-}type}$ or BRCA2$^{-/-}$ cells
Concentration:	0~10 μM
Incubation Time:	7 days
Result:	Showed synthetic lethality and a combinatorial effect with the PARPi olaparib in previously described isogenic models of BRCA1-deficiency.

Western Blot Analysis[1]

Cell Line:	BRCA2$^{wild\text{-}type}$ or BRCA2$^{-/-}$ cells
Concentration:	5μM
Incubation Time:	0~72 hours
Result:	Showed γH2AX accumulation in cells.

CUSTOMER VALIDATION

- Nat Methods. 2023 Jul 20.
- Nat Commun. 2023 Mar 13;14(1):1390.
- J Clin Invest. 2023 Mar 28;e165934.
- Cell Rep. 2023 Apr 21;42(5):112428.
- bioRxiv. 2023 Jun 29.

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REFERENCES

[1]. Zatreanu D, et al. Polθ inhibitors elicit BRCA-gene synthetic lethality and target PARP inhibitor resistance. Nat Commun. 2021 Jun 17;12(1):3636.

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