Product Datasheet

RP-2119

Catalog No. **BP-02060** · CAS **2922287-81-6** · Form **free base** · Physical state **solid** · Color **Off-white to yellow** · Version **1.0** · Revision **2026-09-14**

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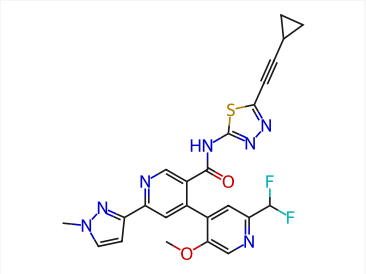
Target	Research area
DNA/RNA Synthesis	**Cancer**

Molecular formula	$C_{24}H_{19}F_2N_7O_2S$
Molecular weight	**507.5150**

STRUCTURE



DESCRIPTION

RP-2119 is an orally bioactive Polymerase Theta (Polθ) inhibitor, with an IC50 of 0.7 nM against human Polθ ATPase. RP-2119 reduces Polθ activity and exerts antiproliferative effects in BRCA2-deficient cancer cells. RP-2119 exhibits antitumor activity in BRCA2-deficient cancer cell xenograft mouse models. RP-2119 can be used for the research of cancer and homologous recombination-deficient cancers, including brca1/brca2-mutant cancers and shld2-mutant cancers.

BIOLOGICAL ACTIVITY

In Vitro

RP-2119 potently inhibits human Polθ ATPase activity in the ADP-Glo biochemical assay, with an IC50 of 0.7 nM. It also inhibits Polθ ATPase activity in mice, rats, dogs, pigs and chimpanzees, with IC50 values ranging from <1.5 nM to <5 nM in the ADP-Glo biochemical assay.

RP-2119 binds to Polθ in K562 cells expressing the ePL-tagged Flag-Polθ helicase domain, with an EC50 of 82 nM in the CETSA assay.

RP-2119 (for 12-14 days) potently inhibits the proliferation of DLD-1, HCT 116 and DOTC24510 BRCA2-/- cells, with EC50 values of 45, 51 and 266 nM.

RP-2119 inhibits Polθ-mediated MMEJ activity in DLD-1 cells carrying Cas9/sgRNA-induced double-strand breaks at the AAVS1 locus, with an IC50 of 54 nM.

In Vivo

RP-2119 (Compound 113) (0-300 mg/kg; p.o.; once/twice daily; throughout the entire study period/24 days) induces dose-dependent tumor growth inhibition in a mouse HCT116 BRCA2-/- colorectal cancer model, with a maximum inhibition rate of 53%, and enhances the tumor volume reduction effect of Olaparib.

RP-2119 (45 mg/kg; p.o.; once daily; for the entire study duration) enhances the tumor volume reduction effect of Carboplatin in a mouse DLD1 BRCA2-/- colorectal cancer model.

Combination treatment with RP-2119 (45 mg/kg; p.o.; twice daily; up to 50 days) and Olaparib induces tumor regression in the BRCA2-mutant mouse HBCx-10 breast cancer PDX model, with significantly enhanced efficacy compared to Olaparib monotherapy.

SOLUBILITY

Soluble in DMSO : 100 mg/mL

REFERENCES

[1]. Bingcan Liu, et al. N-(5-substituted-[(I,3,4-thiadiazolyl) or(I,3-thiazolyl)](substituted)carboxamide compoundspharmaceutical compositions, and methods of preparing the amide compounds and of their use. Wo2024069592A1.2024.04.04.

[2]. Mochirian P, et al. The Discovery of RP-2119: A Potent, Selective, and Orally Bioavailable Polθ ATPase Inhibitor. J Med Chem. 2025;68(18):19726-19745.