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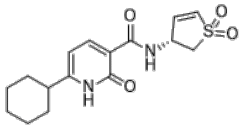
Data Sheet

Global Supplier of Chemical Probes, Inhibitors & Agonists.

Product Name	:	GSK_WRN4
Cat. No.	:	PC-22110
CAS No.	:	2923008-66-4
Molecular Formula	:	$C_{16}H_{20}N_2O_4S$
Molecular Weight	:	336.41
Target	:	DNA Repair Protein
Solubility	:	10 mM in DMSO



CAS: 2923008-66-4

Biological Activity

GSK_WRN4 (WRNi, GSK-WRN4) is a potent and highly selective **WRN helicase** covalent inhibitor with biochemical pIC50 of 7.6, covalently targets WRN Cys727 residue.
GSK_WRN4 displays exceptional specificity for WRN over other RecQ helicases (RecQ5, RecQ1, BLM), significantly modifies WRN Cys727 in Jurkat cells demonstrating the remarkable specificity.
GSK_WRN4 selectively inhibits microsatellite-unstable (MSI) cell growth in vitro and phenocopies genetic inactivation, induces cytotoxic chromosomal instability and DNA damage in MSI cancer cells, by selectively degrading WRN and concurrently upregulating DNA damage response markers such as p-ATM, p-KAP1, p21, and γ-H2AX.
GSK_WRN4 (100 mpk, 300 mpk, p.o.) exerts potent anti-tumor activity in patient-derived xenograft (PDX) model from patient with treatment-refractory MSI CRC, inducing hallmarks of WRN-inhibition-mediated DNA damage.
GSK_WRN4 induces DNA damage specifically in MSI-H, but not other tissues, demonstrating that the in vivo tumor growth inhibition by GSK_WRN4 at 300 mpk is due to WRN helicase inhibition rather than off-target toxicity.

References

Picco G, et al. ***Cancer Discov.*** 2024 Apr 9. doi: 10.1158/2159-8290.CD-24-0052.

E-mail: tech@probechem.com