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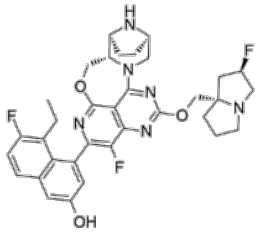
Data Sheet

Global Supplier of Chemical Probes, Inhibitors & Agonists.

Product Name	:	HRS-4642
Cat. No.	:	PC-22656
CAS No.	:	2836263-09-1
Molecular Formula	:	$C_{34}H_{35}F_3N_6O_3$
Molecular Weight	:	632.69
Target	:	Ras
Solubility	:	10 mM in DMSO



CAS: 3033864-81-9

Biological Activity

HRS-4642 is a high affinity, selective, long-acting, and non-covalent **KRAS G12D** inhibitor with SPR KD of 0.083 nM, >20-fold selective over wild-type KRAS and KRAS G12C.
HRS-4642 binds to KRAS G12D in both GDP- and GTP-bound forms.
HRS-4642 selectively inhibits the interaction between GDP-loaded KRAS G12D and SOS1 with IC50 of 0.72 nM.
HRS-4642 inhibits cellular RAS activity in the KRAS G12D-mutant cell line with IC50 of 2.329 nM in AsPC-1 cells, >350-fold selective over PC9 cells.
HRS-4642 selectively hindered the binding of GTP-loaded KRAS G12D to RAF1, a crucial downstream effector of the KRAS signaling pathway with IC50 of 5.9 nM.
HRS-4642 showed dose-dependent inhibition of cellular p-MEK and p-ERK levels in cell lines harboring KRAS G12D mutation.
HRS-4642 exhibited high selectivity in inhibiting the growth of KRAS G12D-mutant cell lines, with IC50 values ranging from 0.55 to 66.58 nM, but not G12C, G12V, G12S, G12A, G13D, and wild type cells.
HRS-4642 (7.5 or 15 mpk) inhibits tumor growth in KRAS G12D-mutant GP2d xenograft model in BALB/c nude mice.

References

Zhou C, et al. ***Cancer Cell.*** 2024 Jul 8;42(7):1286-1300.e8.

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