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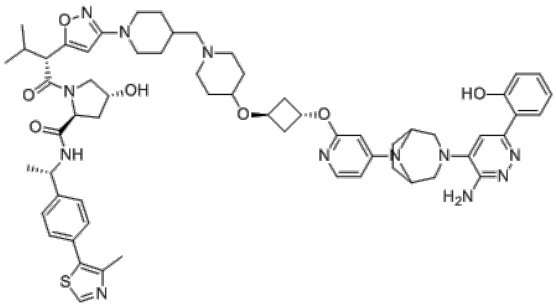
Data Sheet

Global Supplier of Chemical Probes, Inhibitors & Agonists.

Product Name	:	A947
Cat. No.	:	PC-49454
CAS No.	:	2378056-80-3
Molecular Formula	:	$C_{61}H_{76}N_{12}O_7S$
Molecular Weight	:	1121.416
Target	:	PROTAC
Solubility	:	10 mM in DMSO



Biological Activity

A-947 (A947) is a potent and selective **PROTAC** targeting **SMARCA2**, potently degrades SMARCA2 in SW1573 cells with DC50 value of 39 pM, maximal degradation of 96% at 10 nM.
A947 is designed by binding the bromodomains of SMARCA2/4 and PBRM1 to a VHL-targeting moiety, shows binding affinity to the SMARCA2 and SMARCA4 bromodomains with Kd of 93 and 65 nM, respectively.
A947 displays an 28-fold higher concentration needed to achieve a DC50 on SMARCA4 (1.1 nM), with a maximal degradation of SMARCA4 (92%) being achieved at concentrations approaching 100 nM.
A947 also exhibits similar selectivity on SMARCA2 degradation over PBRM1.
Inhibitors of the ubiquitin activating enzyme (MLN-7243) and proteasome inhibitor (MG-132) could block A947-mediated degradation of SMARCA2.
A947 is equally efficient in degrading both the murine and rat orthologs of SMARCA2.
A947 inhibits growth of a panel of SMARCA4-mutant NSCLC cells (mean IC50=7 nM), SMARCA4WT cells is significantly less sensitive to A947 (IC50=86 nM).
A-947 (40 mg/kg, i.v.) exhibits tumor growth inhibition in the SMARCA4wt Calu-6 xenograft model, also shows synergistic effect when combined with MCL1 inhibitor (AMG-176 and S63845).

References

Cantley J, et al. ***Nat Commun***. 2022 Nov 10;13(1):6814.

Caution: Product has not been fully validated for medical applications. Lab Use Only!

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