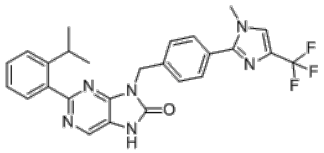
ProbeChem®
Expedite Your Scientific Research

WWW.PROBECHEM.COM

Data Sheet

Global Supplier of Chemical Probes, Inhibitors & Agonists.

Product Name	:	I-138
Cat. No.	:	PC-49689
CAS No.	:	2098211-50-6
Molecular Formula	:	$C_{26}H_{23}F_3N_6O$
Molecular Weight	:	492.51
Target	:	Deubiquitinase (DUB)
Solubility	:	10 mM in DMSO



Biological Activity

I-138 (I 138) is a potent, specific small molecule **USP1-UAF1** inhibitor with IC50 of 4.1 nM, binds to USP1-UAF1 at an allosteric pocket synergistically with ubiquitin.
I-138 displays exquisite selectivity (>2,000-fold) across a panel of 45 deubiquitinating enzymes (Ubiquigent DUBprofiler) at 10 uM, including the closely related USP12-UAF1 and USP46-UAF1 complexes.
I-138 treatment (500 nM, 4 hours) increased PCNA and FANCD2 monoubiquitination in HAP-1 USP1 WT but not knockout cells, induced the monoubiquitination of FANCD2 and PCNA in MDA-MB-436 cells, also ablated USP1 autocleavage in cells.
I-138 (0-10 uM) selectively caused loss of viability (IC50=50 nM) and replication stress in BRCA1/2 mutant cells (MDA-MB-436 cell), but not the WT breast cancer cell line HCC1954.
I-138 displayed improved potency and physiochemical properties suitable for in vivo studies compared with ML323.
I-138 demonstarted strongly synergistic effect with PARP inhibitor Olaparib in a BRCA1/2-dependent manner in vitro, and in mice bearing MDA-MB-436 tumors.

References

Patent WO/2017/087837.

Antoine Simoneau, et al. ***Mol Cancer Ther.*** 2023 Feb 1;22(2):215-226.

E-mail: tech@probechem.com