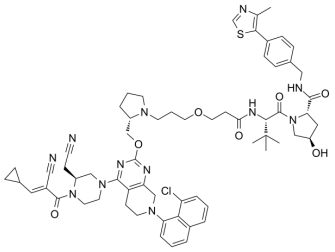
YF135

Cat. No.:	HY-144323
CAS No.:	2913177-53-2
Molecular Formula:	$C_{63}H_{75}ClN_{12}O_7S$
Molecular Weight:	1179.86
Target:	PROTACs; PERK
Pathway:	PROTAC; Cell Cycle/DNA Damage
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

YF135 is an efficient and reversible-covalent $KRAS^{G12C}$ PROTAC. YF135 is designed and synthesized by tethering KRAS G12C inhibitor 48 (compound 6d) as the ligand, and basing on the scaffold of MRTX849 linkage VHL ligand. YF135 significantly induces the degradation of $KRAS^{G12C}$ in a reversible manner and decreases phospho-ERK level through the E3 ligase VHL mediated proteasome pathway[1].

In Vitro

YF135 inhibits the proliferation of H358 and H23 cells with IC_{50} values of 153.9 and 243.9 nM, respectively[1].
YF135 obviously decreases the protein level of $KRAS^{G12C}$ and phospho-ERK in H358 and H23 cells in a time (3 μM, 0-36 h) and dose (0-10 μM, 24 h) dependent manner, while the washout by fresh medium significantly rescues such effects[1].
YF135 induces degradation of $KRAS^{G12C}$ through the E3 ligase VHL mediated proteasome pathway. YF135 covalently bind to $KRAS^{G12C}$ and VHL ligase to form a ternary complex[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis

Cell Line:	lung cancer cell lines H358, H23 and A549 [1]
Concentration:	0, 0.3, 1, 3, 10 μM
Incubation Time:	0, 12, 24, 36 h
Result:	Obviously decreased the protein level of $KRAS^{G12C}$ and phospho-ERK in a time (3 μM, 0-36 h) and dose (0-10 μM, 24 h) dependent manner, with DC_{50} values of 3.61, 1.68 μM in H358 cells, respectively, and 4.53, 1.44 μM in H23 cells, respectively.

Western Blot Analysis

Cell Line:	lung cancer cell lines H358, H23 and A549 [1]
Concentration:	3 μM
Incubation Time:	24 h
Result:	Induced the significant degradation on $KRAS^{G12C}$ and decreased the level of phospho-ERK, while the washout by fresh medium significantly rescued such effects.

REFERENCES

[1]. Yang F, Wen Y, Wang C, et al. Efficient targeted oncogenic KRAS^{G12C} degradation via first reversible-covalent PROTAC. Eur J Med Chem. 2022;230:114088.

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