MS15

Cat. No.: HY-151613

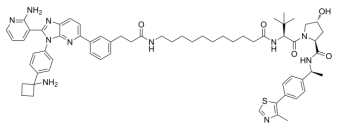
Molecular Formula: $C_{64}H_{79}N_{11}O_5S$

Molecular Weight: 1114.45

Target: Akt; PROTACs

Pathway: PI3K/Akt/mTOR; PROTAC

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

MS15 is a potent and selective AKT PROTAC degrader. MS15 inhibits the AKT1, -2, and -3 activities, with IC_{50} values of 798 nM, 90 nM, and 544 nM, respectively[1].

IC_{50} & Target

Akt2	Akt3	Akt1
90 ± 2.8 nM (IC_{50})	544 ± 2.9 nM (IC_{50})	798 ± 190 nM (IC_{50})

In Vitro

MS15 (0-10 μM, 24 h) potently induces AKT degradation in SW620 cells and MS21-resistant KRAS/BRAF mutant cells[1].
MS15 (0-10 μM, 5 days) inhibits the proliferation of KRAS mutant SW620 cells[1].
MS15 (1 μM, 1-24 h) mediates AKT degradation in a time- and UPS-dependent manner[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	SW620 cells, Colo205, HT-29, SKMEL 239, and PANC-1 cells
Concentration:	1 nM, 3 nM, 10 nM, 30 nM, 100 nM, 300 nM, 1 μM, 3 μM, 10 μM
Incubation Time:	24 h
Result:	Effectively induced T-AKT degradation in a concentration-dependent manner, with a DC_{50} value of 23 ± 16 nM in SW620 cells. Nearly complete AKT degradation was achieved at a concentration of 100 nM in SW620 cells and PANC-1 cells. Induced AKT degradation at 1 μM in BRAF mutant cell lines, such as Colo205, HT-29, and SKMEL 239 cells.

Cell Proliferation Assay[1]

Cell Line:	SW620 cells
Concentration:	0 nM, 30 nM, 100 nM, 1 μM, 3 μM, 10 μM
Incubation Time:	5 days
Result:	Displayed slightly better antiproliferative activity than Miransertib (HY-19719), with a GI_{50} of 3.1 ± 0.3 μM.

In Vivo

MS15 (75 mg/kg, IP, once) is bioavailable in mice through intraperitoneal administration[1].

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Animal Model:	Male Swiss albino mice[1]
Dosage:	75 mg/kg
Administration:	IP, once (Pharmacokinetic Analysis)
Result:	The maximum plasma concentration (Cmax = 1 μM) was achieved at 0.5 h post-treatment, and plasma concentrations were maintained above 100 nM for at least 12 h.Could achieve enough plasma exposure for effective AKT degradation.

REFERENCES

[1]. Yu X, et al. Novel Allosteric Inhibitor-Derived AKT Proteolysis Targeting Chimeras (PROTACs) Enable Potent and Selective AKT Degradation in KRAS/BRAF Mutant Cells. J Med Chem. 2022 Oct 27;65(20):14237-14260.

Caution: Product has not been fully validated for medical applications. For research use only.

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