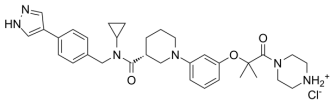
ZW4864

Cat. No.:	HY-132300
CAS No.:	2632259-93-7
Molecular Formula:	$C_{33}H_{43}ClN_6O_3$
Molecular Weight:	607.19
Target:	β-catenin
Pathway:	Stem Cell/Wnt
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	ZW4864 is an orally active and selective β catenin/B-Cell lymphoma 9 protein−protein interaction (β catenin/BCL9 PPI) inhibitor. ZW4864 inhibits β catenin/BCL9 PPI with a K_i value of 0.76 μM and an IC_{50} value of 0.87 μM[1].
IC_{50} & Target	IC50: 0.87 μM (β catenin/BCL9 PPI)[1]. Ki: 0.76 μM(β catenin/BCL9 PPI)[1]
In Vitro	ZW4864 (10~40 μM; 24 hours; SW480 and MBA-MD-231 cells) decreases the expression levels of Axin2 and cyclin D1 proteins [1]. ZW4864 (10~40 μM; 72 hours; MDA-MB231, MCF10A and MDA-MB-468 cells) selectively triggeres rapid apoptosis of triple-negative breast cancer cells with hyperactive β-catenin signaling while sparing normal mammary epithelial MCF10A cells[1]. ZW4864 (10~40 μM; 24 hours; SW480 and MBA-MD-231 cells) suppresses the transcription of β-catenin target genes in a concentration-dependent manner without affecting the expression of HPRT, a house-keeper gene, in both SW480 and Wnt 3a-activated MDA-MB-231 cells[1]. ZW4864 binds with β-catenin and selectively disrupts the protein−protein interaction (PPI) between B-cell lymphoma 9 (BCL9) and β-catenin while sparing the β-catenin/E-cadherin PPI. ZW4864 dose-dependently suppresses β-catenin signaling activation, downregulates oncogenic β-catenin target genes, and abrogates invasiveness of β-catenin-dependent cancer cells. ZW4864 suppresses TOPFlash luciferase activities in β-catenin expressing HEK293 cells in a dose-dependent manner with an IC_{50} of 11 μM. ZW4864 also dose-dependently suppresses the TOPFlash luciferase activities in SW480 and Wnt 3a-activated MDA-MB-468 cells with the IC_{50}s of 7.0 and 6.3 μM, respectively. ZW4864 selectively suppresses transactivation of β-catenin signaling[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	SW480 and MBA-MD-231 cells
Concentration:	10~40 μM
Incubation Time:	24 hours
Result:	Decreased the expression levels of Axin2 and cyclin D1 proteins.

Apoptosis Analysis[1]

Cell Line:	MDA-MB231, MCF10A and MDA-MB-468 cells

Concentration:	10~40 μM
Incubation Time:	72 hours
Result:	Selectively triggered rapid apoptosis of triple-negative breast cancer cells with hyperactive β-catenin signaling while sparing normal mammary epithelial MCF10A cells.

RT-PCR[1]

Cell Line:	SW480 and MBA-MD-231 cells
Concentration:	10~40 μM
Incubation Time:	24 hours
Result:	Suppressed the transcription of β-catenin target genes in a concentration-dependent manner without affecting the expression of HPRT, a house-keeper gene, in both SW480 and Wnt 3a-activated MDA-MB-231 cells.

In Vivo

ZW4864 (20 mg/kg; p.o.) exhibits good pharmacokinetic properties with an oral bioavailability (F) of 83 %[1].
ZW4864 (90 mg/kg; p.o.) shows a variation in tumor growth in mice[1].
ZW4864 shows good pharmacokinetic properties and effectively suppresses β-catenin target gene expression in the patient-derived xenograft mouse model[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	C57BL/6 mice[1]
Dosage:	20 mg/kg (Pharmacokinetic Analysis)
Administration:	P.o.
Result:	Exhibited good pharmacokinetic properties with an oral bioavailability (F) of 83%.

Animal Model:	Mice[1]
Dosage:	90 mg/kg
Administration:	P.o.
Result:	Showed a variation in tumor growth in mice.

REFERENCES

[1]. Wang Z, et al. Discovery of an Orally Bioavailable Small-Molecule Inhibitor for the β-Catenin/B-Cell Lymphoma 9 Protein-Protein Interaction. J Med Chem. 2021;64(16):12109-12131.

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

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