PROTAC TTK degrader-2

Cat. No.: HY-143905

CAS No.: 2953426-48-5

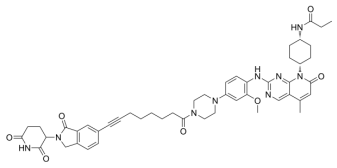
Molecular Formula: $C_{49}H_{57}N_9O_7$

Molecular Weight: 884.03

Target: PROTACs

Pathway: PROTAC

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



BIOLOGICAL ACTIVITY

Description

PROTAC TTK degrader-2 is a potent TTK (threonine tyrosine kinase) PROTAC degrader, with DC_{50} values of 3.1 and 12.4 nM in COLO-205 and HCT-116 cell, respectively. PROTAC TTK degrader-2 exhibits target degradation and anticancer efficacy in a xenograft mouse model of COLO-205 human colorectal cancer cells[1].

IC_{50} & Target

DC_{50}: 3.1 nM (TTK) in COLO-205, 12.4 nM (TTK) in HCT-116[1]

In Vitro

PROTAC TTK degrader-2 (compound 8j) (0-10 μM, 96 h) inhibits cancer cell proliferation[1].

PROTAC TTK degrader-2 (5 and 50 nM, 6 h) induces degradation of TTK protein in a dose-dependent manner[1].

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

Cell Proliferation Assay

Cell Line:	COLO-205 and HCT-116 cells[1]
Concentration:	0-10 μM
Incubation Time:	96 h
Result:	Inhibited the growth of COLO-205 cancer cells with an IC_{50} of 0.2 μM.

Western Blot Analysis

Cell Line:	COLO-205, HCT-116 LOVO, HCT-8, and HCT-29 human colon cancer cell lines[1]
Concentration:	5, 50 nM
Incubation Time:	6 h
Result:	Induced degradation of TTK protein in a dose-dependent manner.

In Vivo

PROTAC TTK degrader-2 (8j) (10 mg/kg, IP, single) demonstrates reasonable pharmacokinetics profiles[1].

PROTAC TTK degrader-2 (10, 20 mg/kg, IP, once daily for 16 days) significantly reduces the TTK protein levels, and exhibits tumor-growth inhibition[1].

Pharmacokinetic Parameters of PROTAC TTK degrader-2 in male SD rats[1].

	8j
AUC (ng/mL*h)	2333
$T_{1/2}$ (h)	3.2

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

Animal Model:	Male SD rats (, three animals per group)[1]
Dosage:	10 mg/kg, dissolved in mixed solvents (5% 20 mg/mL DMSO stock, 30% PG, 30% PEG400, and 35% Saline)
Administration:	IP, single (Pharmacokinetic Analysis)
Result:	Demonstrated reasonable pharmacokinetics profiles.

Animal Model:	Male CB17-SCID mice (xenograft mouse model of COLO-205 cells)[1]
Dosage:	10, 20 mg/kg
Administration:	IP, once daily for 16 days
Result:	Significantly reduced the TTK protein levels in animal tumor tissues, exhibited tumor-growth inhibition value of 36.7% upon 20 mg/kg dosing, did not cause a significant body weight loss of the animal.

REFERENCES

[1]. Lu J, Huang Y, Huang J, et al. Discovery of the First Examples of Threonine Tyrosine Kinase PROTAC Degraders. J Med Chem. 2022;65(3):2313-2328.

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