PROTAC TTK degrader-1

Cat. No.: HY-143904

CAS No.: 2953426-43-0

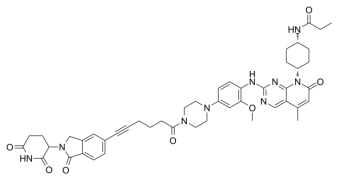
Molecular Formula: $C_{47}H_{53}N_9O_7$

Molecular Weight: 855.98

Target: PROTACs

Pathway: PROTAC

Storage: 4°C, protect from light
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (116.83 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.1683 mL	5.8413 mL	11.6825 mL
	5 mM	0.2337 mL	1.1683 mL	2.3365 mL
	10 mM	0.1168 mL	0.5841 mL	1.1683 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

PROTAC TTK degrader-1 is a potent TTK (threonine tyrosine kinase) PROTAC degrader, with DC_{50} values of 1.7 and 5.8 nM in COLO-205 and HCT-116 cell, respectively. PROTAC TTK degrader-1 exhibits target degradation and anticancer efficacy in a xenograft mouse model of COLO-205 human colorectal cancer cells[1].

IC_{50} & Target

DC_{50}: 1.7 nM (TTK) in COLO-205, 5.8 nM (TTK) in HCT-116[1]

In Vitro

PROTAC TTK degrader-1 (compound 8e) (0-10 μM, 96 h) inhibits cancer cell proliferation[1].
PROTAC TTK degrader-1 (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 0.1 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-1 (10 mg/kg, IP, single) demonstrates reasonable pharmacokinetics profiles[1].
PROTAC TTK degrader-1 (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-1 in male SD rats[1].

	8e
AUC (ng/mL*h)	2235
$T_{1/2}$ (h)	4.3

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

Animal Model:	Male SD rats[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 (bearing COLO-205 tumor xenografts)[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 46.0% 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.

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

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