OTUB1/USP8-IN-1

Cat. No.: HY-151563

CAS No.: 2858800-98-1

Molecular Formula: $C_{22}H_{16}ClFN_2O_4$

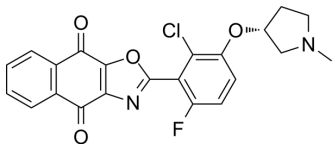
Molecular Weight: 426.82

Target: Deubiquitinase

Pathway: Cell Cycle/DNA Damage

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (117.15 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3429 mL	11.7145 mL	23.4291 mL
	5 mM	0.4686 mL	2.3429 mL	4.6858 mL
	10 mM	0.2343 mL	1.1715 mL	2.3429 mL

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

BIOLOGICAL ACTIVITY

Description

OTUB1/USP8-IN-1 is a potent dual OTUB1/USP8 inhibitor with IC_{50} values of 0.17 and 0.28 nM for OTUB1 and USP8, respectively. OTUB1/USP8-IN-1 can be used in research of cancer[1].

IC_{50} & Target

IC50: 0.17 nM (OTUB1) and 0.28 nM (USP8)[1]

In Vitro

OTUB1/USP8-IN-1 (compound 61; 10 nM-10 μM; 72 h) has antiproliferative effects in KRAS-WT (H1975, EBC-1, H1703) and KRAS-mutated (H23, A549) NSCLC cell lines[1].

OTUB1/USP8-IN-1 (500 nM; 24 h) decreases in protein levels of both UBE2N and EGFR in H1975 cells[1].

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

Cell Viability Assay[1]

Cell Line:	KRAS-WT (H1975, EBC-1, H1703) and KRAS-mutated (H23, A549) NSCLC cell lines
Concentration:	10 nM-10 μM

Incubation Time:	72 hours
Result:	Inhibited cell proliferative with IC_{50} values of 118, 145, 172, 431, and 1004 nM for H1975, H1703, EBC-1, H23, and A549 cells, respectively.

Western Blot Analysis[1]

Cell Line:	H1975 cells
Concentration:	500 nM
Incubation Time:	24 hours
Result:	Decreased the levels of both UBE2N and EGFR in a dose-dependent manner.

In Vivo

OTUB1/USP8-IN-1 (compound 61; 10 nM-10 μM; 72 h) decreases the tumor burden in the H1975 xenograft mouse model[1].

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

Animal Model:	Female BALB/c nude mice with H1975 xenografts (5 weeks of age)[1]
Dosage:	5 mg/kg
Administration:	Intraperitoneal injection; QD and BID, for 2 weeks
Result:	Reduced total tumor weight and average tumor volume in an over twofold with BID dosing.

Animal Model:	Female BALB/c nude mice with H1975 xenograft (5 weeks of age)[1]
Dosage:	1 and 10 mg/kg
Administration:	Intravenous injection (1 mg/kg) and oral administration (10 mg/kg)

Result:

Administration	i.v. (1 mg/kg)	p.o. (10 mg/kg)
$T_{1/2}$ (h)	0.83	1.75
T_{max} (h)		0.33
C_{max} (μg/L)		4274
AUC (μg·h/L)	1345	3747
CL (L/h/kg)	44	
Vdss (L/kg)	0.77	

REFERENCES

[1]. Tan L, et, al. Discovery of Potent OTUB1/USP8 Dual Inhibitors Targeting Proteostasis in Non-Small-Cell Lung Cancer. J Med Chem. 2022 Oct 11.

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