PROTAC Axl Degrader 2

Cat. No.: HY-144627

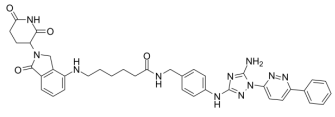
Molecular Formula: $C_{38}H_{39}N_{11}O_4$

Molecular Weight: 713.79

Target: PROTACs; TAM Receptor

Pathway: PROTAC; Protein Tyrosine Kinase/RTK

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (140.10 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.4010 mL	7.0049 mL	14.0097 mL
	5 mM	0.2802 mL	1.4010 mL	2.8019 mL
	10 mM	0.1401 mL	0.7005 mL	1.4010 mL

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

BIOLOGICAL ACTIVITY

Description

PROTAC Axl Degrader 2 is a potent and selective PROTAC Axl degrader with an IC_{50} of 1.61 μM. PROTAC Axl Degrader 2 shows anti-proliferation activity, anti-migration activity in vitro. PROTAC Axl Degrader 2 induces mehuosis[1].

IC_{50} & Target

IC_{50}: 1.61 μM (AXL)[1]

In Vitro

PROTAC Axl Degrader 2 (compound 20) (72 h) shows anti-proliferation activity with IC_{50}s of 6.23 μM, 2.06 μM, for MDA-MB-231, 4T1 cells, respectively[1].
PROTAC Axl Degrader 2 (0.5, 2 μM; 24, 48 h) decreases the abundance of AXL in MDA-MB-231 cells[1].
PROTAC Axl Degrader 2 (1, 2 μM) reduces the expression of AXL, can be restored in the presence of EPO (epoxymycin)[1].
PROTAC Axl Degrader 2 (1, 10 μM; 48 h) significantly inhibits the migration in MDA-MB-231 and 4T1 cells[1].
PROTAC Axl Degrader 2 (0.5 μM) induces cytoplasmic vacuolation (methuosis) in MDA-MB-231 and 4T1 cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	MDA-MB-231, 4T1, GES-1, MCF-10A cells

Concentration:	
Incubation Time:	72 h
Result:	Showed anti-proliferation activity with IC_{50}s of 6.23 μM, 2.06 μM, for MDA-MB-231, 4T1 cells, respectively.

Western Blot Analysis[1]

Cell Line:	MDA-MB-231 cells
Concentration:	0.5, 2 μM
Incubation Time:	24, 48 h
Result:	Decreased AXL abundance in MDA-MB-231 cells.

In Vivo

PROTAC Axl Degrader 2 (25 mg/kg, i.p.) dose not induce systemic toxicity[1].
PROTAC Axl Degrader 2 (20 mg/kg for o.p.; 2 mg/kg for i.v.) shows an oral bioavailability of 7.80%[1].
Pharmacokinetic Parameters of PROTAC Axl Degrader 2 in 6 weeks, 180-220g, male Sprague-Dawley (SD) rats[1].

Cmds	Rout	Dose (mg/kg)	AUC_{0-t} (ng·h/mL)	C_{max} (ng/mL)	T_{max} (h)	$T_{1/2}$ (h)	CL (L/h/kg)	BA (%)
20	i.v.	2	7581.3	279	0.82	1.18	0.72	-
	p.o.	20	3592.1	144	2.25	4.43	-	7.80

6 weeks, 180-220g, male Sprague-Dawley (SD) rats; 20 mg/kg for o.p.; 2 mg/kg for i.v.
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female balb/c nude mice (MDA-MB-231 xenografts)[1]
Dosage:	25 mg/kg
Administration:	Intraperitoneal injection
Result:	Did not induce systemic toxicity.

Animal Model:	6 weeks, 180-220g, male Sprague-Dawley (SD) rats[1]
Dosage:	
Administration:	20 mg/kg for o.p.; 2 mg/kg for i.v.
Result:	Showed an oral bioavailability of 7.80%.

REFERENCES

[1]. Shi W, et al. Structure-based discovery of receptor tyrosine kinase AXL degraders with excellent anti-tumor activity by selectively degrading AXL and inducing methuosis. Eur J Med Chem. 2022; 234:114253.

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

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