PROTAC Axl Degrader 1

Cat. No.: HY-144624

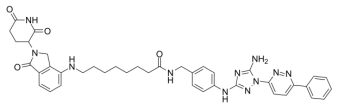
Molecular Formula: $C_{40}H_{43}N_{11}O_4$

Molecular Weight: 741.84

Target: PROTACs; TAM Receptor

Pathway: PROTAC; Protein Tyrosine Kinase/RTK

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



BIOLOGICAL ACTIVITY

Description

PROTAC Axl Degrader 1 is a potent and selective PROTAC Axl degrader with an IC_{50} of 0.92 μM. PROTAC Axl Degrader 1 shows anti-proliferation activity, anti-migration activity in vitro. PROTAC Axl Degrader 1 induces mehuosis[1].

IC_{50} & Target

IC_{50}: 0.92 μM (AXL)[1]

In Vitro

PROTAC Axl Degrader 1 (compound 22) (72 h) shows anti-proliferation activity with IC_{50}s of 10.34 μM, 5.53 μM, for MDA-MB-231, 4T1 cells, respectively[1].
PROTAC Axl Degrader 1 (0.5, 2 μM; 24, 48 h) decreases the abundance of AXL in MDA-MB-231 cells[1].
PROTAC Axl Degrader 1 (1, 2 μM) reduces the expression of AXL, could be restored in the presence of EPO (epoxymycin)[1].
PROTAC Axl Degrader 1 (1, 10 μM; 48 h) significantly inhibits the migration in MDA-MB-231 and 4T1 cells[1].
PROTAC Axl Degrader 1 (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 10.34 μM, 5.53 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 1 (25 mg/kg, i.p.) dose not induce systemic toxicity[1].
PROTAC Axl Degrader 1 (20 mg/kg for o.p.; 2 mg/kg for i.v.) shows an oral bioavailability of 4.93%[1].

Pharmacokinetic Parameters of PROTAC Axl Degrader 1 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 (%)
22	i.v.	2	2933.4	166	0.54	0.72	0.68	-
	p.o.	20	864.7	92	1.89	2.37	-	4.93

6 weeks, 180-220g, male Sprague-Dawley (SD) rats; 20 mg/kg for o.p.; 2 mg/kg for i.v.[1].

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

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.

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