(4S)-PROTAC SOS1 degrader-1

Cat. No.: HY-144657

CAS No.: 2913176-81-3

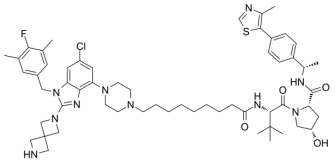
Molecular Formula: $C_{57}H_{76}ClFN_{10}O_4S$

Molecular Weight: 1051.79

Target: PROTACs; Ras

Pathway: PROTAC; GPCR/G Protein

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



BIOLOGICAL ACTIVITY

Description

(4S)-PROTAC SOS1 degrader-1 is a potent PROTAC SOS1 degrader. (4S)-PROTAC SOS1 degrader-1 decreases the expression of pERK and RAS-GTP level in a dose-dependent manner. (4S)-PROTAC SOS1 degrader-1 significantly inhibits the tumor growth in vivo[1].

IC_{50} & Target

K-RAS

In Vitro

(4S)-PROTAC SOS1 degrader-1 (compound 9d) (0.1, 1 μM) shows a potent SOSI degradation activity with an SOS1 protein degradation of 56.2 and 92.5% at 0.1 and 1 μM in NCI-H358 cells, respectively[1].
(4S)-PROTAC SOS1 degrader-1 (24 h) degrades SOS1 in a dose- and time-dependent manner in NCI-H358 cells[1].
(4S)-PROTAC SOS1 degrader-1 (9.8-2500 nM; 24 h) does not induce SOS2 and KRAS degradation in NCI-H358 cells[1].
(4S)-PROTAC SOS1 degrader-1 (7.8-2000 nM; 24 h) decreases the expression of pERK and RAS-GTP level in NCI-H358 cells in a dose-dependent manner[1].

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

Western Blot Analysis[1]

Cell Line:	NCI-H358 cells
Concentration:	7.8, 15.6, 31.2, 62.5, 125, 250, 500, 1000, 2000 nM
Incubation Time:	24 h
Result:	Showed a potent degradation activity with an EC_{50} of 98.4 nM in NCI-H358 cells.

RT-PCR[1]

Cell Line:	NCI-H358 cells
Concentration:	1 μM
Incubation Time:	24, 48, 72 h
Result:	Showed the SOS2 mRNA level remained constant during the incubation period.

Cell Proliferation Assay[1]

Cell Line:	NCI-H358, MIA PaCa2, AsPC-1, SK-LU-1, SW620, A549 cells
Concentration:	0-10000 nM
Incubation Time:	7 days
Result:	Inhibited the cell growth with IC_{50}s of 0.525, 0.218, 0.307, 0.115, 0.199, 0.232 μM (EC_{50}s of 0.098, 0.255, 0.119, 0.104, 0.125, 0.022 μM)for NCI-H358, MIA PaCa2, AsPC-1, SK-LU-1, SW620, A549 cells, respectively.

In Vivo

PROTAC SOS1 degrader-2 (10, 20 mg/kg; i.p., daily for 21 days) significantly inhibits the tumor growth in vivo with a good safety profile[1].

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

Animal Model:	BALB/c nude mice (NCI-H358 tumor xenografts)[1]
Dosage:	10, 20 mg/kg
Administration:	I.p.; daily, 21 days
Result:	Significantly inhibited the tumor growth in vivo with a good safety profile.

REFERENCES

[1]. Zhou C,et al. Discovery of the First-in-Class Agonist-Based SOS1 PROTACs Effective in Human Cancer Cells Harboring Various KRAS Mutations. J Med Chem. 2022; 65(5):3923-3942.

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