SIAIS117

Cat. No.: HY-146022

CAS No.: 2353494-84-3

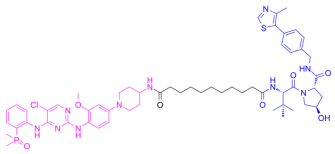
Molecular Formula: $C_{57}H_{76}ClN_{10}O_7PS$

Molecular Weight: 1111.77

Target: PROTACs; Anaplastic lymphoma kinase (ALK)

Pathway: PROTAC; Protein Tyrosine Kinase/RTK

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



BIOLOGICAL ACTIVITY

Description

SIAIS117 is a potent Brigatinib-PROTAC degrader. SIAIS117 is a ALK PROTAC based on Brigatinib and VHL-1 conjunction. SIAIS117 can degrade ALK G1202R point mutation effectively. SIAIS117 blocks the growth of SR and H2228 cancer cell lines. SIAIS117 has the potentially anti-proliferation ability of small cell lung cancer[1].

In Vitro

SIAIS117 (0-10 μM, 72 h) inhibits SR, H2228, NCI-H69 and NCI-H1688 cell growth, with IC_{50} values of 1.7, 46, 799, and 259 nM, respectively[1].

SIAIS117 (0-500 nM, 24 h) inhibits the phosphorylation of ALK and STAT3[1].

SIAIS117 inhibits the growth of G1202R-mutant ALK cell line and degrades G1202R-ALK protein[1].

SIAIS117 (100 nM, 24 h) causes sustained degradation of ALK protein in SR cells[1].

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

Cell Proliferation Assay

Cell Line:	NSCLC cell line H2228, Small cell lung cancer cell lines (NCI-H69, NCI-H1688)[1]
Concentration:	0-10 μM
Incubation Time:	72 h
Result:	Inhibited cell growth with an about two folds lower IC_{50} value (46 nM) comparing to SIAIS117NC (114 nM). Showed a good growth inhibition effect on NCI-H69 and NCI-H1688 cell line, with IC_{50} values of 799 and 259 nM, respectively.

Western Blot Analysis

Cell Line:	SR, H2228[1]
Concentration:	0, 1, 10, 50, 100, 500 nM
Incubation Time:	24 h
Result:	Inhibited all of the phosphorylation of ALK at 10 nM and inhibited pSTAT3 in SR cell, degraded ALK proteins at the concentration starting from 50 nM in H2228 cell, and significantly downregulated UCK2 and GAK. Caused sustained degradation of ALK protein in SR cells.

REFERENCES

[1]. Sun N, Ren C, Kong Y, et al. Development of a Brigatinib degrader (SIAIS117) as a potential treatment for ALK positive cancer resistance. Eur J Med Chem. 2020;193:112190.

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