SIAIS164018

Cat. No.: HY-147219

CAS No.: 2353492-68-7

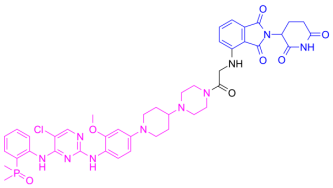
Molecular Formula: $C_{43}H_{48}ClN_{10}O_7P$

Molecular Weight: 883.33

Target: PROTACs; Anaplastic lymphoma kinase (ALK); EGFR; Apoptosis

Pathway: PROTAC; Protein Tyrosine Kinase/RTK; JAK/STAT Signaling; Apoptosis

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (113.21 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.1321 mL	5.6604 mL	11.3208 mL
	5 mM	0.2264 mL	1.1321 mL	2.2642 mL
	10 mM	0.1132 mL	0.5660 mL	1.1321 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (2.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SIAIS164018 is a PROTAC-based ALK and EGFR degrader, with IC_{50} value of 2.5 nM and 6.6 nM for ALK and ALK G1202R, respectively. SIAIS164018 strongly inhibits cancer cells migration and invasion, causes G1 cell cycle arrest and induces apoptosis. SIAIS164018 exhibits better property than Brigatinib (HY-12857)[1].

IC_{50} & Target

IC_{50}: 2.5 nM (ALK), 6.6 nM (ALK G1202R)[1]

In Vitro

SIAIS164018 (0-1 μM; 16 h) significantly inhibits SR cell proliferation[1].
SIAIS164018 (0-100 nM; 72 h) shows better cell proliferation inhibition than Brigatinib does in ALK (G1202R) over-expressing 293T and EGFR expressing H1975 cell lines[1].
SIAIS164018 (100 nM; 24 or 48 h) induces a significant G1 cell cycle arrest in ALK-negative Calu-1 and MDA-MB-231 cells[1].
SIAIS164018 (0.01-1000 nM; 16h) down-regulates the protein level of FAK, PYK2, FER, RSK1, and GAK in ALK-positive SR and ALK-negative Calu-1 cell lines[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	SR cells
Concentration:	0-1 μM
Incubation Time:	16 h
Result:	Significantly inhibited SR cell proliferation with an IC_{50} value of 2 nM.

Cell Proliferation Assay[1]

Cell Line:	ALK (G1202R) over-expressing 293T and EGFR expressing H1975 cell lines
Concentration:	0-100 nM
Incubation Time:	72 h
Result:	Exhibited better cell proliferation inhibition than Brigatinib does in ALK (G1202R) over-expressing 293T and EGFR expressing H1975 cell lines with IC_{50}s 21 and 42 nM, respectively.

Cell Cycle Analysis[1]

Cell Line:	ALK-negative Calu-1 and MDA-MB-231 cells
Concentration:	100 nM
Incubation Time:	24 or 48 h
Result:	Induced a significant G1 cell cycle arrest in ALK-negative Calu-1 and MDA-MB-231 cells.

Western Blot Analysis[1]

Cell Line:	SR and Calu-1 cells
Concentration:	0.01, 0.1, 1, 10, 100 and 1000 nM
Incubation Time:	16 h
Result:	Down-regulated the protein level of FAK, PYK2, FER, RSK1, and GAK.

REFERENCES

[1]. Ren C, et al. Discovery of a Brigatinib Degrader SIAIS164018 with Destroying Metastasis-Related Oncoproteins and a Reshuffling Kinome Profile. J Med Chem. 2021 Jul 8;64(13):9152-9165.

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