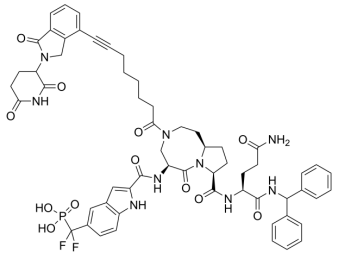
SD-36

Cat. No.:	HY-129602
CAS No.:	2429877-44-9
Molecular Formula:	$C_{59}H_{62}F_2N_9O_{12}P$
Molecular Weight:	1158.15
Target:	PROTACs; STAT; Apoptosis
Pathway:	PROTAC; JAK/STAT Signaling; Stem Cell/Wnt; Apoptosis
Storage:	-20°C, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (43.17 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	0.8634 mL	4.3172 mL	8.6345 mL
	5 mM	0.1727 mL	0.8634 mL	1.7269 mL
	10 mM	0.0863 mL	0.4317 mL	0.8634 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.25 mg/mL (1.08 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.25 mg/mL (1.08 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (1.08 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SD-36 is a potent and efficacious STAT3 PROTAC degrader (K_d=~50 nM), and demonstrates high selectivity over other STAT members. SD-36 also effectively degrades mutated STAT3 proteins in cells and suppresses the transcriptional activity of STAT3 (IC_{50}=10 nM). SD-36 exerts robust anti-tumor activity, and achieves complete and long-lasting tumor regression in mouse tumor models. SD-36 is composed of the STAT3 inhibitor SI-109, a linker, and an analog of Cereblon ligand Lenalidomide for E3 ubiquitin ligase[1].

IC_{50} & Target		
	STAT3 50 nM (Kd)	Cereblon

In Vitro

SD-36 inhibits the growth of a subset of acute myeloid leukemia and anaplastic large-cell lymphoma cell lines by inducing cell-cycle arrest and/or apoptosis[1].

SD-36 (0.005-5 μM; 4 days) demonstrates potent activity (IC_{50}≤2 μM) in MOLM-16, DEL, Karpas-299, KI-JK, SU-DHL-I, SUP-M2 cell lines[1].

SD-36 (1 μM; 5 hours) completely depletes both monomeric and dimeric STAT3 protein in MOLM-16 cells[1].

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

Cell Viability Assay[1]

Cell Line:	MOLM-16, DEL, Karpas-299, KI-JK, SU-DHL-I, SUP-M2 cell lines
Concentration:	0.005, 0.05, 0.5, 5 μM
Incubation Time:	4 days
Result:	Demonstrated potent activity (IC_{50}≤2 μM) in those cell lines.

Western Blot Analysis[1]

Cell Line:	MOLM-16 cells
Concentration:	1 μM
Incubation Time:	5 hours
Result:	Completely depletes both monomeric and dimeric STAT3 protein.

In Vivo

SD-36 (25-100 mg/kg; i.v.; weekly dosing for 4 weeks) achieves complete and long-lasting tumor regression in mice[1].

?SD-36 effectively inhibits tumor growth at 25 and 50 mg/kg administered on day 1, 3, and 5 per week and achieved complete tumor regression at 100 mg/kg with the same schedule in the SU-DHL-1 xenograft model[1].

?SD-36 at 50 mg/kg 3 times per week completely inhibits tumor growth in the SUP-M2 tumor model[1].

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

Animal Model:	SCID female mice (MOLM-16 xenograft model)[1]
Dosage:	25, 50, 100 mg/kg
Administration:	i.v.; weekly dosing for 4 weeks
Result:	At 25 and 50 mg/kg weekly dosing for 4 weeks effectively inhibited tumor growth. At either 100 mg/kg weekly or 50 mg/kg twice weekly for 4 weeks induced complete tumor regression.

CUSTOMER VALIDATION

- Sci Transl Med. 2023 Jun 28;15(702):eabo3826.
- J Cell Mol Med. 2021 Jul 21.

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REFERENCES

[1]. Bai L, et al. A Potent and Selective Small-Molecule Degrader of STAT3 Achieves Complete Tumor Regression In Vivo. Cancer Cell. 2019 Nov 11;36(5):498-511.e17.

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