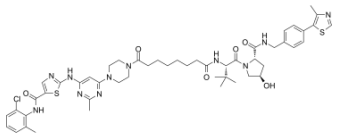
SIAIS178

Cat. No.:	HY-128756
CAS No.:	2376047-73-1
Molecular Formula:	$C_{50}H_{62}ClN_{11}O_6S_2$
Molecular Weight:	1012.68
Target:	PROTAC; Bcr-Abl
Pathway:	PROTAC; Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 300 mg/mL (296.24 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	0.9875 mL	4.9374 mL	9.8748 mL
	5 mM	0.1975 mL	0.9875 mL	1.9750 mL
	10 mM	0.0987 mL	0.4937 mL	0.9875 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: ≥ 7.5 mg/mL (7.41 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SIAIS178 is a potent and selective BCR-ABL degrader based on PROTAC technology with an IC_{50} of 24 nM. SIAIS178 causes effective degradation of BCR-ABL protein by recruiting Von Hippel-Lindau (VHL) E3 ubiquitin ligase. SIAIS178 has anticancer activity[1].

IC_{50} & Target		
	VHL	Bcr-Abl 24 nM (IC_{50})

In Vitro

SIAIS178 (1-100 nM; for 16 hours) significantly reduces the BCR-ABL protein levels in a concentration dependent manner. SIAIS178 significantly inhibits the phosphorylation of BCR-ABL and the substrates STAT5[1].

SIAIS178 (1, 10, 100, 1000 nM) exerts significant antiproliferative activity in BCR-ABL driven CML cell lines. SIAIS178 retains potency and selectivity against the BCR-ABL driven cell lines[1].

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

Western Blot Analysis[1]

Cell Line:	K562 cells
Concentration:	1, 3, 10, 30, 100 nM
Incubation Time:	16 hours
Result:	Significantly reduced the BCR-ABL protein levels in a concentration dependent manner.

In Vivo

SIAIS178 (ip; 5, 15, and 45 mg/kg; 12 days) attenuates tumor progression in a dose-dependent manner, as determined by serial volumetric measurement [1].

SIAIS178 (iv or ip; 2 mg/kg; 24 hours) has $T_{1/2}$ of 3.82 and 12.35 hours and C_{max} of 1165.2 nM and 30 nM for iv and ip, respectively[1].

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

Animal Model:	NOD/SCID mice with termed K562-Luc[1]
Dosage:	5, 15, and 45 mg/kg
Administration:	Ip; 12 days
Result:	Attenuated tumor progression in a dose-dependent manner, as determined by serial volumetric measurement.

Animal Model:	Female Wistar rats[1]
Dosage:	2 mg/kg (Pharmacokinetic Analysis)
Administration:	Iv or ip; 24 hours
Result:	Had $T_{1/2}$ of 3.82 and 12.35 hours and C_{max} of 1165.2 nM and 30 nM for iv and ip, respectively.

REFERENCES

[1]. Zhao Q, et al. Discovery of SIAIS178 as an Effective BCR-ABL Degrader by Recruiting Von Hippel-Lindau (VHL) E3 Ubiquitin Ligase. J Med Chem. 2019 Oct 24;62(20):9281-9298.

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