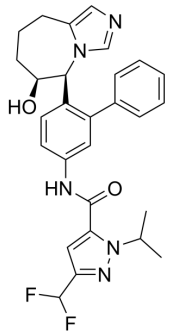
CSN5i-3

Cat. No.:	HY-112134
CAS No.:	2375740-98-8
Molecular Formula:	$C_{28}H_{29}F_2N_5O_2$
Molecular Weight:	505.56
Target:	Others
Pathway:	Others
Storage:	-20°C, protect from light, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light, stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (197.80 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9780 mL	9.8900 mL	19.7800 mL
	5 mM	0.3956 mL	1.9780 mL	3.9560 mL
	10 mM	0.1978 mL	0.9890 mL	1.9780 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: ≥ 2.5 mg/mL (4.95 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.95 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	CSN5i-3 is a potent, selective and orally available inhibitor of CSN5/Jab1, and inhibits CSN-catalysed Cul1 deneddylation with an IC_{50} value of 5.8 nM[1].
IC_{50} & Target	IC50: 5.8 nM (CSN5)[1]
In Vitro	CSN5i-3 traps CRLs in the neddylated state, which leads to inactivation of a subset of CRLs by inducing degradation of their substrate recognition module[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	CSN5i-3 shows a good pharmacokinetic profile. Treatment with CSN5i-3 triggers the formation of cleaved PARP and cleaved

	caspase 3 indicative of apoptosis induction[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay	Cell viability is measured using the CellTiter-Glo Assay. Cells (THP-1, HCT116, NCI-H2030 and TE-1) are treated with CSN5i-3 (1 nM, 10 nM, 100 nM, 1 μM, 10 μM) for 72 hours[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] SU-DHL-1 xenografts were grown in SCID-bg mice and dosed by oral administration with either vehicle control or CSN5i-3 at the indicated doses (50 mg/kg BID, 100mg/kg QD) and schedules (3, 7, 10, 14 day). Tumour response is reported as percentage change in tumour volume at the last day of treatment relative to start of treatment. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell. 2023 Apr 27;186(9):1895-1911.e21.
- Sci Immunol. 2021 Apr 30;6(58):eabe2933.
- Mol Cell. 2023 Feb 10;S1097-2765(23)00042-4.
- Biochem Biophys Res Commun. 2022.
- Research Square Preprint. 2023 May 3.

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REFERENCES

[1]. Schlierf A, et al. Targeted inhibition of the COP9 signalosome for treatment of cancer. Nat Commun. 2016 Oct 24;7:13166.

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