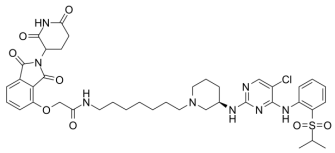
BSJ-4-116

Cat. No.:	HY-139039
CAS No.:	2519823-34-6
Molecular Formula:	$C_{40}H_{49}ClN_8O_8S$
Molecular Weight:	837.38
Target:	CDK; PROTACs
Pathway:	Cell Cycle/DNA Damage; PROTAC
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 : 250 mg/mL (298.55 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.1942 mL	5.9710 mL	11.9420 mL
	5 mM	0.2388 mL	1.1942 mL	2.3884 mL
	10 mM	0.1194 mL	0.5971 mL	1.1942 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: ≥ 2.08 mg/mL (2.48 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (2.48 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BSJ-4-116 is a PROTAC connected by ligands for Cereblon and CDK. BSJ-4-116 is a highly potent and selective CDK12 degrader (PROTAC) with an IC_{50} of 6 nM. BSJ-4-116 downregulates DDR genes through a premature termination of transcription, primarily through increasing poly(adenylation). BSJ-4-116 exhibits potent antiproliferative effects, alone and in combination with the poly(ADP-ribose) polymerase inhibitor Olaparib (HY-10162)[1].

IC_{50} & Target		
	CDK12 6 nM (IC_{50})	Cereblon

In Vitro

BSJ-4-116 (10-10000 nM; 72 hours) exhibits potent antiproliferative effects in Kelly $CDK12^{C1039F}$[1].
BSJ-4-116 (50 nM; 6-24 hours) decreases the level of CDK12 protein, regardless of the mutational status of the cell line[1].

BSJ-4-116 inhibits the growth of T-ALL cells (Jurkat and MOLT-4 cells) and sensitizes them to PARP inhibition[1].
BSJ-4-116 regulates DDR genes via poly(adenylation). BSJ-4-116 overcomes CDK12^{C1039F} mutation. BSJ-4-116 represents the first example of resistance to a bivalent degrader molecule that is a consequence of an acquired point mutation in the target protein[1].

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

Cell Proliferation Assay[1]

Cell Line:	Parental Kelly and CDK12^{C1039F} cells
Concentration:	10-10000 nM
Incubation Time:	72 hours
Result:	Antiproliferative activity of BSJ-4-116 is independent of the mutational status, and the degrader compounds exhibited improved GR_{50} (growth rate inhibition) values in Kelly CDK12^{C1039F} cells compared with the parental cell line.

Western Blot Analysis[1]

Cell Line:	Parental and CDK12^{C1039F} (KellyCDK12CF)-expressing Kelly cells
Concentration:	50 nM
Incubation Time:	6-24 hours
Result:	Led to the same level of CDK12 protein level decrease, regardless of the mutational status of the cell line.

REFERENCES

[1]. Jiang B, et al. Discovery and resistance mechanism of a selective CDK12 degrader. Nat Chem Biol. 2021;17(6):675-683.

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