SJ988497

Cat. No.: HY-151902

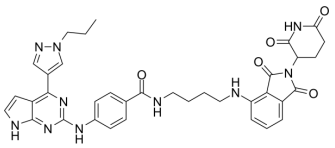
CAS No.: 2595365-41-4

Molecular Formula: $C_{36}H_{36}N_{10}O_5$

Molecular Weight: 688.74

Target: PROTACs; JAK

Pathway: PROTAC; Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt



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 : 33.33 mg/mL (48.39 mM; ultrasonic and warming and heat to 80°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.4519 mL	7.2596 mL	14.5193 mL
	5 mM	0.2904 mL	1.4519 mL	2.9039 mL
	10 mM	0.1452 mL	0.7260 mL	1.4519 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 (3.63 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

SJ988497 is a PROTAC JAK2 degrader. SJ988497 potently inhibits CRLF2-rearranged (CRLF2r) cell proliferation and degrades the CRBN neosubstrate GSPT1. SJ988497 consists of a Ruxolitinib (HY-50856) derivative, linker, and CRBN ligand Pomalidomide. SJ988497 can be used in the research of acute lymphoblastic leukemia (ALL)[1].

IC_{50} & Target

JAK2

In Vitro

SJ988497 (compound 7) increases cell permeability in the Caco-2 assay, with the apparent permeability coefficient (P_{app}) of 19.12 nm/s[1].

SJ988497 inhibits parental MHH-CALL-4 cells with an EC_{50} of 0.4 nM, inhibits CRBN-KD MHH–CALL-4 cells with an EC_{50} of 3456.2 nM, and can be blocked by 30 μM Lenalidomide (HY-A0003)[1].

SJ988497 (1 h, 1 μM) results in comparable JAK inhibition in MHH–CALL-4 cells[1].

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

Cell Viability Assay[1]

Cell Line:	NAL M6, MHH-CALL-2, 697, KOPN49, KOPN75, MHH-CALL-4 cells
Concentration:	0.01 nM-100 nM
Incubation Time:	72 h
Result:	Dose-dependently inhibited cell viability in ALL cell lines.

Western Blot Analysis[1]

Cell Line:	MHH-CALL-4 cells
Concentration:	1 nM, 10 nM, 100 nM, 1 μM, 4 μM.
Incubation Time:	1 h
Result:	Degraded multiple JAKs (JAK1>JAK3>JAK2>TYK2), and was abolished by knockdown of CRBN.

In Vivo

SJ988497 (compound 7) (30 mg/kg, i.p.) reduces spleen size and tumor burdens, and is well tolerated with no weight loss or perturbation in blood count[1].

SJ988497 (10-100 mg/kg, i.p., twice daily) showed sustained in vivo exposure with the plasma concentration above the cellular 50% effective concentration value after 24 hour[1].

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

Animal Model:	NSG mice inoculated by CL20SF2-Luc2aYFP cell (i.v.)[1]
Dosage:	30 mg/kg
Administration:	Intraperitoneal injection (i.p.)
Result:	Reduced leukemia burden in bone marrow, blood, and spleen, as well as total body bioluminescent imaging.

REFERENCES

[1]. Chang Y, et al. Degradation of Janus kinases in CRLF2-rearranged acute lymphoblastic leukemia. Blood. 2021 Dec 9;138(23):2313-2326.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA