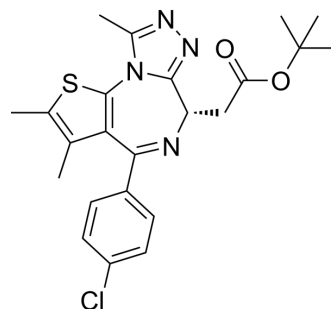


(+)-JQ-1

Cat. No.:	HY-13030
CAS No.:	1268524-70-4
Molecular Formula:	C ₂₃ H ₂₅ ClN ₄ O ₂ S
Molecular Weight:	456.99
Target:	Epigenetic Reader Domain; Autophagy; Ligands for Target Protein for PROTAC
Pathway:	Epigenetics; Autophagy; PROTAC
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 1 year -20°C 6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 45 mg/mL (98.47 mM)
 * "≥" means soluble, but saturation unknown.

	Solvent Concentration	Mass	1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM		2.1882 mL	10.9412 mL	21.8823 mL
	5 mM		0.4376 mL	2.1882 mL	4.3765 mL
	10 mM		0.2188 mL	1.0941 mL	2.1882 mL

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

In Vivo

- Add each solvent one by one: 15% Cremophor EL >> 85% Saline
Solubility: 10 mg/mL (21.88 mM); Clear solution; Need ultrasonic
- Add each solvent one by one: 20% HP-β-CD in saline
Solubility: 10 mg/mL (21.88 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.5 mg/mL (5.47 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.5 mg/mL (5.47 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (5.47 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

(+)-JQ-1 (JQ1) is a potent, specific, and reversible BET bromodomain inhibitor, with IC₅₀s of 77 and 33 nM for the first and second bromodomain (BRD4(1/2))^[1]. (+)-JQ-1 also activates autophagy^[2].

IC ₅₀ & Target	IC ₅₀ : 77/33 nM (BRD4(1/2)) ^[1]
In Vitro	(+)-JQ-1 represents a potent, highly specific and Kac competitive inhibitor for the BET family of bromodomains. (+)-JQ-1 (100 nM, 48 h) prompts squamous differentiation exhibited by cell spindling, flattening and increased expression of keratin. (+)-JQ-1 (250 nM) induces rapid expression of keratin in treated NMC 797 cells compared to (-)-JQ1 (250 nM) and vehicle controls, as determined by quantitative immunohistochemistry. (+)-JQ-1 (250 nM) elicits a time-dependent induction of strong (3+) keratin staining of treated NMC 797 cells, compared to (-)-JQ1 (250 nM)^[1]. De-repression of autophagy genes is observed almost immediately after (+)-JQ-1 addition^[2]. (+)-JQ-1 is a potent thienodiazepine inhibitor (K_d=90 nM) of the BET family coactivator protein BRD4, which is implicated in the pathogenesis of cancer via transcriptional control of the MYC oncogene. Dose-ranging studies of (+)-JQ-1 demonstrates potent inhibition of H4Kac4 binding with a IC₅₀ value of 10 nM for murine BRDT(1) and 11 nM for human BRDT(1)^[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Matched cohorts of mice with established tumors are randomized to treatment with (+)-JQ1 (50 mg/kg) or vehicle, administered by daily intraperitoneal injection. Prior to randomization, and after four days of therapy, mice are evaluated by FDG-PET imaging. A marked reduction in FDG uptake is observed with (+)-JQ1 treatment. Tumor-volume measurements confirm a reduction in tumor growth with JQ1 treatment. Pharmacokinetic studies of (+)-JQ1 are performed in CD1 mice following intravenous and oral administration. Mean plasma concentration-time profiles of (+)-JQ1 after intravenous dosing (5 mg/kg). The pharmacokinetic parameters for intravenous (+)-JQ1 demonstrate excellent drug exposure (AUC=2090 hr*ng/mL) and an approximately one hour half-life (T_{1/2}). Mean plasma concentration-time profiles of (+)-JQ1 after oral dosing (10 mg/kg). The pharmacokinetic parameters for oral (+)-JQ1 demonstrate excellent oral bioavailability (F=49%), peak plasma concentration (C_{max}=1180 ng/mL) and drug exposure (AUC=2090 hr*ng/mL)^[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay ^[1]	NUT midline carcinoma patient cell lines (797 and 11060) are plated in T-25 flasks and grown in DMEM (797) or RPMI (11060) containing 10 % fetal bovine serum. Cells are treated with either 250 nM (+)-JQ1, 250 nM (-)-JQ1 or the equivalent volume of DMSO (0.025%). At the desired time point, 2×10⁶ cells are spun at 500× g for 5 minutes at 4°C and washed with PBS. Pellets are resuspended in 1 mL of cold PBS and added dropwise while gently vortexing to 9 mL 70 % ethanol in a 15 mL polypropylene centrifuge tube. Fixed cells are then frozen at -20°C overnight. The next day, cells are centrifuged at 500× g for 10 minutes at 4°C and washed with 3 mL of cold PBS. Cells are resuspended in 500 µL of propidium iodide staining solution (0.2 mg/mL RNase A, 0.02 mg/mL propidium iodide, 0.1 % Triton-X in PBS) and incubated for 20 minutes at 37°C. Samples are then transferred to ice and analyzed on a BD FACS Canto II. Histograms are generated and cell cycle analysis is performed using FlowJo flow cytometry analysis software^[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration ^{[1][3]}	Mice^[1] Matched cohorts of mice with established tumors are randomized to treatment with (+)-JQ1 (50 mg/kg) or vehicle, administered by daily intraperitoneal injection. Male CD1 mice (24-29 g) are treated with a single dose of (+)-JQ1 at 5 mg/kg for intravenous tail vein injection studies and 10 mg/kg for oral gavage studies. Rats^[3] Adult male Sprague-Dawley rats are treated with vehicle or (+)-JQ1 (10 mg/kg). Treatment is administered IP at 1/100 body mass. Rats are checked twice-daily for mortality and weighed on days 1, 3, 7, 14, and 21. The treatment regimen utilized 4 days of 50 mg/kg JQ1 administered daily which is decreased to 10 mg/kg twice daily for the remainder of the study due to the appearance of adverse effects in a subset of animals. For all animals completing 3 weeks of treatment, testis mass, sperm motility, and sperm counts are determined as described for mouse studies. In brief, testes are fixed in Bouin's and prepared for histology. The other half is minced in warm M16 buffer and used for sperm counts and motility studies. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell. 2018 Sep 20;175(1):186-199.e19.
- Cancer Cell. 2018 Feb 12;33(2):274-291.e8.
- Cell Res. 2022 Apr 15.
- Mol Cancer. 2023 Mar 30;22(1):64.
- Mol Cancer. 2020 Sep 9;19(1):139.

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REFERENCES

- [1]. Filippakopoulos P, et al. Selective inhibition of BET bromodomains. Nature. 2010 Dec 23;468(7327):1067-73.
- [2]. Sakamaki JI, et al. Bromodomain Protein BRD4 Is a Transcriptional Repressor of Autophagy and Lysosomal Function. Mol Cell. 2017 May 18;66(4):517-532.e9.
- [3]. Matzuk MM, et al. Small-molecule inhibition of BRDT for male contraception. Cell. 2012 Aug 17;150(4):673-84.
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Caution: Product has not been fully validated for medical applications. For research use only.

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