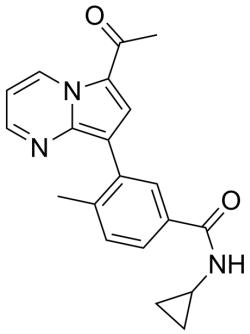
TP-472

Cat. No.:	HY-100517
CAS No.:	2079895-62-6
Molecular Formula:	$C_{20}H_{19}N_3O_2$
Molecular Weight:	333.38
Target:	Epigenetic Reader Domain; Apoptosis
Pathway:	Epigenetics; Apoptosis
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 : 100 mg/mL (299.96 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.9996 mL	14.9979 mL	29.9958 mL
5 mM	0.5999 mL	2.9996 mL	5.9992 mL
10 mM	0.3000 mL	1.4998 mL	2.9996 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 (7.50 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.50 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TP-472 is a selective BRD9/7 inhibitor, with K_ds of 33 nM and 340 nM for BRD9 and BRD7, respectively. TP-472 exhibits >30-fold selectivity for BRD9 over other bromodomain family members except BRD7[1][2]. TP-472 induces apoptosis of melanoma cells[3].

IC_{50} & Target

BRD9	BRD7
33 nM (Kd)	0.34 μM (Kd)

In Vitro

TP-472 (1 μM, 3 μM; 24-216 hours) yields concentration-dependent growth defects in ESCs[2].
TP-472 (0.1-10 μM; 24 h) effectively inhibits the growth of both the BRAF mutant melanoma cell lines at 5 and 10 μM concentrations[3].

TP-472 (for 2 weeks) also strongly inhibits the long-term survival of multiple melanoma cell lines (M14, SKMEL-28, A375, and A2058) at concentrations of 5 and 10 μM[3].
TP-472 (5-10 μM; 24 h) treatment downregulates genes encoding various extracellular matrix (ECM) proteins, including integrins, collagens, and fibronectins in A375 cells[3].
TP-472 (0.1-10 μM; 24 h) results in the upregulation of pro-apoptotic genes (BAX, MDM2, CDKN1A) in A375 cells[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[2]

Cell Line:	Embryonic stem cells
Concentration:	1 μM, 3 μM
Incubation Time:	24 hours, 72 hours, 120 hours, 168 hours, 216 hours
Result:	Yields concentration-dependent growth defects in ESCs.

Cell Proliferation Assay[3]

Cell Line:	M14 and SKMEL-28 cells[3]
Concentration:	0.1 μM, 0.5 μM, 1 μM, 2 μM, 5 μM, 10 μM
Incubation Time:	24 h
Result:	Effectively inhibited the growth of both the BRAF mutant melanoma cell lines.

Western Blot Analysis[3]

Cell Line:	A375 cells
Concentration:	10 μM
Incubation Time:	24 h
Result:	Resulted in the upregulation of pro-apoptotic genes.

In Vivo

TP-472 (20 mg/kg; i.p.; three times a week; for 5 weeks) significantly inhibits the subcutaneous tumor growth in melanoma xenograft mouse model[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	NSG mice injected with A375-MA2 cells (male five- to six-week-old)[3]
Dosage:	20 mg/kg
Administration:	i.p.; three times a week; for 5 weeks
Result:	Significantly inhibited the subcutaneous tumor growth in melanoma xenograft mouse model.

REFERENCES

[1]. Lawrence David Mason, et al. The BRD9/7 Inhibitor TP-472 Blocks Melanoma Tumor Growth by Suppressing ECM-Mediated Oncogenic Signaling and Inducing Apoptosis. Cancers (Basel). 2021 Nov 3;13(21):5516.

[2]. Gatchalian J, et al. A non-canonical BRD9-containing BAF chromatin remodeling complex regulates naive pluripotency in mouse embryonic stem cells. Nat Commun. 2018 Dec 3;9(1):5139.

[3]. Moustakim M, et al. Chemical probes and inhibitors of bromodomains outside the BET family. Medchemcomm. 2016 Dec 7;7(12):2246-2264.

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