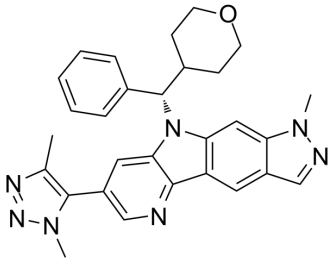
NHWD-870

Cat. No.:	HY-134463
CAS No.:	2115742-03-3
Molecular Formula:	$C_{29}H_{29}N_7O$
Molecular Weight:	491.59
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 : 62.5 mg/mL (127.14 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0342 mL	10.1711 mL	20.3422 mL
	5 mM	0.4068 mL	2.0342 mL	4.0684 mL
	10 mM	0.2034 mL	1.0171 mL	2.0342 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 (4.23 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.23 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

NHWD-870 is a potent, orally active and selective BET family bromodomain inhibitor and only binds bromodomains of BRD2, BRD3, BRD4 (IC_{50}=2.7 nM), and BRDT. NHWD-870 has potent tumor suppressive efficacies and suppresses cancer cell-macrophage interaction. NHWD-870 increases tumor apoptosis and inhibits tumor proliferation[1].

In Vitro

NHWD-870 (0.01-10000 nM) inhibits melanoma cells (A375) with an IC_{50} of 2.46 nM[1].
NHWD-870 (0-10000 nM; 5 dys) suppressed cell growth[1].
NHWD-870 (0-50 nM; 24 hours) inhibits BRD4 phosphorylation and c-MYC expression[1].
NHWD-870 exhibits mild inhibition of hERG channel (IC_{50} = 5.4 μM)[1].NHWD-870 shows robust activities inducing apoptosis and suppressing cell proliferation[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	H526, A2780, ES-2, and MDA-MB231 cells
Concentration:	0-10000 nM
Incubation Time:	5 days
Result:	Showed strong inhibitory activities against these cells in 5-day assays.

Western Blot Analysis[1]

Cell Line:	H526, A2780, ES-2, and MDA-MB231 cells
Concentration:	0-50 nM
Incubation Time:	24 hours
Result:	Led to the depletion of phosphorylated BRD4 and c-MYC at 10 nM.

In Vivo

NHWD-870 (0.75-3 mg/kg; p.o.) has strong anti-tumor activities in mouse models[1].
NHWD-870 reduces the number of tumor associated macrophages (TAMs) in subcutaneously implanted H526 and A2780 tumors. NHWD-870 downregulated CSF1 expression in tumor cells to inhibit TAM proliferation[1].
NHWD-870 manifests diverse mechanisms of action in different cancer settings. These include: 1) inhibition of tumor cell growth by downregulating the PDGFRβ, MEK1/2 and STAT1/MYC signaling in tumor cells; 2) inhibition of tumor angiogenesis by decreasing PDGF production in tumor cells and the PDGFRβ and MEK1/2 signaling in endothelial cells. NHWD-870 has potent tumor suppressive efficacies in xenograft mouse models of small cell lung cancer, triple negative breast cancer and ovarian cancer[2].
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Animal Model:	4-6 weeks old female BALB/c nude mice/6-8 weeks old female C57BL/6 mice were used for B16F10 experiments (bearing NCI-H526, A2780, A375, B16F10, and TMD-8 cells)[1]
Dosage:	0.75-3 mg/kg
Administration:	P.o.; TMD8 and B16F10 melanoma model with once daily for 11-21 days; A375 melanoma and PDX of melanoma with once daily (5 days on, 2 days off) for 21 days.
Result:	Strongly suppressed the growth of established lung tumor, ovarian tumor, lymphoma, and melanoma in vivo.

REFERENCES

[1]. Yin M, et al. Potent BRD4 inhibitor suppresses cancer cell-macrophage interaction. Nat Commun. 2020;11(1):1833. Published 2020 Apr 14.

[2]. Nenghui Wang, et al. Abstract 1382: A novel BET family bromodomain inhibitor NHWD-870 represents a promising therapeutic agent for a broad spectrum of cancers. Molecular and Cellular Biology, Genetics.

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