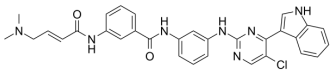
THZ2

Cat. No.:	HY-12280
CAS No.:	1604810-84-5
Molecular Formula:	$C_{31}H_{28}ClN_7O_2$
Molecular Weight:	566.05
Target:	CDK
Pathway:	Cell Cycle/DNA Damage
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 21.67 mg/mL (38.28 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7666 mL	8.8331 mL	17.6663 mL
	5 mM	0.3533 mL	1.7666 mL	3.5333 mL
	10 mM	0.1767 mL	0.8833 mL	1.7666 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: ≥ 2.17 mg/mL (3.83 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.17 mg/mL (3.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

THZ2 is a potent and selective CDK7 inhibitor with an IC_{50} of 13.9 nM.

IC_{50} & Target

CDK7 13.9 nM (IC_{50})	CDK1 96.9 nM (IC_{50})	CDK2 222 nM (IC_{50})	CDK5 134 nM (IC_{50})
CDK9 194 nM (IC_{50})	CDK8 6830 nM (IC_{50})		

In Vitro

THZ2 selectively targets CDK7 and potently inhibits the growth of triple-negative but not ER/PR^+ breast cancer cells. THZ2 at low nanomolar doses also efficiently suppresses the clonogenic growth of TNBC cells with IC_{50} of appr 10 nM. THZ2 induces

	apoptotic cell death in triple-negative but not ER/PR$^+$ breast cancer cells or normal human cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	THZ2 (10 mg/Kg) markedly reduces the growth rate of tumors in mice and demonstrates an anti-tumor activity. Compared to vehicle-treated tumors, tumor tissues isolated from mice treated with THZ2 has reduced proliferation and increased apoptosis, as indicated by immunostaining against Ki67 and cleaved Caspase 3 respectively. THZ2 in NOD-SCID mice leads to reduced body weight, suggesting that THZ2 mayt be less well-tolerated in this particular mouse strain[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	For 96-well plate assay, cells are plated at the density of 2000 cells per well, and on the next day treated with THZ1 or THZ2 of various concentrations. After 48-hour incubation, cells are fixed and stained with crystal violet. The staining is then extracted by adding each well with 10% acetic acid, with absorbance measured at 590 nm with 750 nm as a reference. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Nude mice (CrTac:NCr-Foxn1nu) are γ-irradiated with a single dose of 400 rads six hours before transplantation of cells. Breast cancer cells are harvested and resupended in 40% Matrigel-Basement Membrane Matrix, LDEV-free, and then injected (100 μL per site) into the fourth pair of mammary fat pads of mice. Tumors are measured in two dimensions by using manual calipers. Tumor volume is calculated using the formula: V=0.5× length × width × width. Animal with tumor established (mean tumor volume of appr 200 mm^3) are randomLy divided into two groups, which are then treated with vehicle (10% DMSO in D5W, 5% dextrose in water) or THZ2 (3 mg/mL, prepared in vehicle solutions) at the dose of 10 mg/kg intraperitoneally twice daily. Tumor volume is measure every 2-3 days. Upon harvesting tumors, tumors are cut into half, with one half fixed in formalin overnight and then in 70% ethanol for histopathology analysis, and the other half snap frozen in liquid nitrogen for immunoblotting. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Cell Biol. 2020 Aug;22(8):986-998.
- bioRxiv. 2020 Apr.

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REFERENCES

[1]. Wang Y, et al. CDK7-Dependent Transcriptional Addiction in Triple-Negative Breast Cancer. Cell. 2015 Sep 24;163(1):174-186.

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