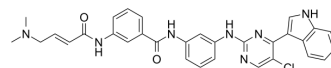


## THZ2

Cat. No.:	HY-12280		
CAS No.:	1604810-84-5		
Molecular Formula:	C <sub>31</sub> H <sub>28</sub> ClN <sub>7</sub> O <sub>2</sub>		
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)			
		Solvent Concentration	Mass	
			1 mg	5 mg
	Preparing Stock Solutions	1 mM	1.7666 mL	8.8331 mL
	5 mM	0.3533 mL	1.7666 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 <sub>50</sub> of 13.9 nM.			
IC <sub>50</sub> & Target	CDK7	CDK1	CDK2	CDK5
	13.9 nM (IC <sub>50</sub> )	96.9 nM (IC <sub>50</sub> )	222 nM (IC <sub>50</sub> )	134 nM (IC <sub>50</sub> )
	CDK9	CDK8		
	194 nM (IC <sub>50</sub> )	6830 nM (IC <sub>50</sub> )		
In Vitro	THZ2 selectively targets CDK7 and potently inhibits the growth of triple-negative but not ER/PR <sup>+</sup> breast cancer cells. THZ2 at low nanomolar doses also efficiently suppresses the clonogenic growth of TNBC cells with IC <sub>50</sub> of appr 10 nM. THZ2 induces			

apoptotic cell death in triple-negative but not ER/PR<sup>+</sup> breast cancer cells or normal human cells<sup>[1]</sup>.  
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 may be less well-tolerated in this particular mouse strain<sup>[1]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

#### Cell Assay <sup>[1]</sup>

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 <sup>[1]</sup>

Mice: Nude mice (CrTac:NCr-Foxn1nu) are  $\gamma$ -irradiated with a single dose of 400 rads six hours before transplantation of cells. Breast cancer cells are harvested and resuspended in 40% Matrigel-Basement Membrane Matrix, LDEV-free, and then injected (100  $\mu$ L 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:  $V=0.5 \times \text{length} \times \text{width} \times \text{width}$ . Animal with tumor established (mean tumor volume of approx 200 mm<sup>3</sup>) 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 measured 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.

**Caution: Product has not been fully validated for medical applications. For research use only.**

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