# ZSTK474

Cat. No.:	HY-50847		
CAS No.:	475110-96-	4	
Molecular Formula:	$C_{19}H_{21}F_2N_7O_2$		
Molecular Weight:	417.41		
Target:	PI3K; Autophagy; Autophagy		
Pathway:	PI3K/Akt/m	TOR; Aut	ophagy
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year

®

MedChemExpress

## SOLVENT & SOLUBILITY

In Vitro	DMSO : 2 mg/mL (4.79 mM; Need ultrasonic)				
Preparing Stock Solutions		Mass Solvent Concentration	1 mg	5 mg	10 mg
	1 mM	2.3957 mL	11.9786 mL	23.9573 mL	
	5 mM				
		10 mM			
	Please refer to the so	lubility information to select the app	propriate solvent.		
In Vivo	1. ZSTK474 is susper	nded in 5% hydroxypropyl cellulose <sup>[</sup>	3].		

Diologicite				
Description	ZSTK474 is an ATP-competitiv δ and PI3Kγ, respectively.	re pan-class I PI3K inhibitor with	IC <sub>50</sub> s of 16 nM, 44 nM, 4.6 nM and	49 nM for ΡΙ3Κα, ΡΙ3Κβ, ΡΙ3Κ
IC₅₀ & Target	ΡΙ3Κδ 4.6 nM (IC <sub>50</sub> )	ΡΙ3Κα 16 nM (IC <sub>50</sub> )	ΡΙ3Κβ 44 nM (IC <sub>50</sub> )	ΡΙ3Κγ 49 nM (IC <sub>50</sub> )
	Autophagy			
In Vitro	Lineweaver-Burk plot analysis values determined for the fou 1.8 nM, whereas the other isof pan-PI3K inhibitor. We also de IC <sub>50</sub> values of ZSTK474 (16, 44	s revealed that ZSTK474 inhibits r PI3K isoforms showed that ZST forms are inhibited with 4-10-fold etermined the IC <sub>50</sub> values for inhi ., 4.6 and 49 nM for PI3Kα, PI3Kβ,	all four PI3K isoforms in an ATP-c K474 inhibited the PI3Kδ isoform I higher K <sub>i</sub> values. Therefore, ZST biting the four PI3K isoforms with PI3Kδ and PI3Kγ, respectively) ar	ompetitive manner. The K <sub>i</sub> most effectively with a K <sub>i</sub> of K474 should be regarded as a n ZSTK474 and LY294002. The re shown to be consistent

F

Ο

	with the K <sub>i</sub> values (6.7, 10.4, 1.8 and 11.7 nM for PI3Kα, PI3Kβ, PI3Kδ and PI3Kγ, respectively), which further supported the idea that ZSTK474 inhibits PI3Kδ most potently. Even at a concentration of 100 μM, ZSTK474 inhibits mTOR activity rather weakly <sup>[1]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In mice subjected to MCAO, treatment with ZSTK474 is tested at dosages of 50, 100, 200, and 300 mg/kg. Since the 200 mg/kg dose produces significant improvement and no obvious toxic effects (P<0.01), mice are treated with ZSTK474 at a dose of 200 mg/kg/day daily for three post-MCAO days during the remaining experiments of this study. Neurological function is examined in mice suffered from MCAO followed by 24, 48, and 72 h of reperfusion. In the ZSTK474 group, neurological function scores are significantly better than the control group except the corner test <sup>[2]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only.

### PROTOCOL

Kinase Assay <sup>[1]</sup>	The linear phase of each kinetic reaction is defined at the respective enzyme amount (0.05, 0.1, 0.12 and 1 $\mu$ g/mL for PI3Ka, PI3 $\beta$ , PI3 $\delta$ and PI3 $\gamma$ , respectively) and reaction time (20 min). PI3K activity is assayed at various concentrations of ATP (5, 10, 25, 50, 100 $\mu$ M) in the presence of increasing concentrations of ZSTK474. A Lineweaver-Burk plot is developed by plotting 1/v (the inverse of v, where v is obtained by subtracting the HTRF signal of the kinase test sample from the HTRF signal of the minus-enzyme control) versus 1/[ATP] (the inverse of the ATP concentration). For the minus-enzyme control, PIP2 is incubated with ATP in the absence of kinase. To determine the K <sub>i</sub> value (inhibition constant) of ZSTK474 for each PI3K isoform, the slope of the respective Lineweaver-Burk plot is replotted against the ZSTK474 concentration. The K <sub>i</sub> values are calculated by analysis using GraphPad Prism 4 <sup>[1]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal	Mice <sup>[2]</sup>
Administration <sup>[2]</sup>	Mice are randomly assigned to receive different doses of ZSTK474 (50, 100, 200, and 300 mg/kg) to determine the optimum dose; in our experiment, the optimum dose is 200 mg/kg. Then mice are randomly assigned to one of three groups: a sham-operated group (phosphate-buffered saline, PBS); a control group (MCAO+PBS); a ZSTK474-treated group (MCAO+ZSTK474). In the ZSTK474-treated group, the mice are given the optimum dose of 200 mg/kg ZSTK474. In the sham-operated group and control group, mice are given an equivalent volume of PBS. All mice receive that same dose daily via oral gavage beginning at 6 h after the onset of focal ischemia and continuing for two more days, i.e., for a total of 3 days.

### CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Clin Cancer Res. 2014 Nov 1;20(21):5483-95.
- J Exp Clin Cancer Res. 2018 Jun 25;37(1):122.
- Cell Syst. 2020 Jan 22;10(1):66-81.e11.
- Mol Metab. 2023 Mar 10;101705.

See more customer validations on <u>www.MedChemExpress.com</u>

#### REFERENCES

[1]. Kong D, et al. ZSTK474 is an ATP-competitive inhibitor of class I phosphatidylinositol 3 kinase isoforms. Cancer Sci, 2007, 98(10), 1638-1642.

[2]. Wang P, et al. Class I PI3K inhibitor ZSTK474 mediates a shift in microglial/macrophage phenotype and inhibits inflammatory response in mice with cerebral

ischemia/reperfusion injury. J Neuroinflammation. 2016 Aug 22;13(1):192.

[3]. Liu F, et al. Prolonged inhibition of class I PI3K promotes liver cancer stem cell expansion by augmenting SGK3/GSK-3β/β-catenin signalling. J Exp Clin Cancer Res. 2018 Jun 25;37(1):122.

#### 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