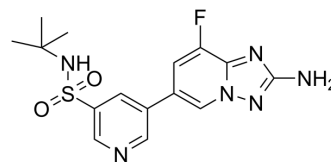


## CZC24832

<b>Cat. No.:</b>	HY-15294		
<b>CAS No.:</b>	1159824-67-5		
<b>Molecular Formula:</b>	C <sub>15</sub> H <sub>17</sub> FN <sub>6</sub> O <sub>2</sub> S		
<b>Molecular Weight:</b>	364.4		
<b>Target:</b>	PI3K		
<b>Pathway:</b>	PI3K/Akt/mTOR		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : ≥ 53 mg/mL (145.44 mM)  
 \* "≥" means soluble, but saturation unknown.

	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.7442 mL	13.7212 mL	27.4424 mL
	5 mM	0.5488 mL	2.7442 mL	5.4885 mL
	10 mM	0.2744 mL	1.3721 mL	2.7442 mL

Please refer to the solubility information to select the appropriate solvent.

#### In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
 Solubility: 2.5 mg/mL (6.86 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
 Solubility: 2.5 mg/mL (6.86 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
 Solubility: ≥ 2.5 mg/mL (6.86 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

CZC24832 is a highly selective and potent PI3K $\gamma$  inhibitor (IC<sub>50</sub>=27 nM) with apparent dissociation constants (K<sub>d</sub><sup>app</sup>) of 19 nM.

#### IC<sub>50</sub> & Target

PI3K $\gamma$ 27 nM (IC <sub>50</sub> )	PI3K $\beta$ 1.1 $\mu$ M (IC <sub>50</sub> )	PI3K $\delta$ 8.194 $\mu$ M (IC <sub>50</sub> )
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<b>In Vitro</b>	CZC24832 is active in PI3K $\gamma$ -dependent cellular C5a-induced AKT Ser473 phosphorylation (IC <sub>50</sub> =1.2 $\mu$ M) and N-formyl-methionine-leucinephenylalanine (fMLP)-induced neutrophil migration assays (IC <sub>50</sub> =1.0 $\mu$ M) <sup>[1]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
<b>In Vivo</b>	CZC24832 shows suitable pharmacokinetic properties including low clearance (0.84 L per h per kg body weight) and high oral bioavailability (37%), thus allowing further characterization of the inhibitor in rodent models of inflammation. In an IL-8-dependent air pouch model, CZC24832 shows a dose-dependent reduction of granulocyte recruitment (80% inhibition at 10 mg per kg body weight) consistent with the degree of inhibition observed in PI3K $\gamma$ -null mice. Mice treated orally with 10 mg CZC24832 per kg body weight twice per day show a substantial decrease of bone and cartilage destruction (53% reduction by histopathological analysis) as well as of overall clinical parameters (38% reduction) <sup>[1]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

<b>Cell Assay</b> <sup>[1]</sup>	RAW264.7 or THP-1 cells are starved for 2.5 h in serum-free medium before CZC24832 (0.1, 1, 10 and 100 $\mu$ M) incubation for 30 min at 37°C. RAW264.7 cells are then stimulated for 3 min with C5a at a concentration of 0.6 $\mu$ M, and THP-1 cells are stimulated with either insulin (1 $\mu$ M, 10 min) or CSF (50 $\mu$ g/mL, 5 min) at 37°C and lysed on ice. The detection of AKT phosphorylation (Ser473) is performed using the iBlot system <sup>[1]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
<b>Animal Administration</b> <sup>[1]</sup>	Rats <sup>[1]</sup> Pharmacokinetics and oral bioavailability of CZC24832 are investigated in male Wistar rats following administration of a single intravenous (0.2 mg per kg body weight) or oral dose (10 mg per kg body weight). The dosing vehicle used is 0.5% (w/v) carboxymethyl cellulose in water for oral gavage. The intravenous dosing vehicle is 10% (v/v) DMSO in 30% (v/v) polyethylene glycol (PEG-400). Heparin blood for pharmacokinetic analysis is withdrawn retro-orbitally from mice or sublingually from rats to prepare plasma samples. These are homogenized with 10% (v/v) water and 3 volumes of acetonitrile and analyzed for CZC24832 by HPLC-MS/MS. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## REFERENCES

[1]. Bergamini G, et al. A selective inhibitor reveals PI3K $\gamma$  dependence of T(H)17 cell differentiation. Nat Chem Biol. 2012 Apr 29;8(6):576-82.

**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