# **Product** Data Sheet



# CCT128930

Cat. No.: HY-13260 CAS No.: 885499-61-6 Molecular Formula: C18H20CIN5 Molecular Weight: 341.84

Target: Akt; Autophagy; Apoptosis

Pathway: PI3K/Akt/mTOR; Autophagy; Apoptosis

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: 33.33 mg/mL (97.50 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent Mass Concentration	1 mg	5 mg	10 mg	
	1 mM	2.9253 mL	14.6267 mL	29.2535 mL	
	5 mM	0.5851 mL	2.9253 mL	5.8507 mL	
	10 mM	0.2925 mL	1.4627 mL	2.9253 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 (6.08 mM); Clear solution
- 2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.08 mg/mL (6.08 mM); Clear solution
- 3. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.08 mg/mL (6.08 mM); Clear solution

# **BIOLOGICAL ACTIVITY**

Description	CCT128930 is a ATP-competitive and selective inhibitor of AKT (IC $_{50}$ =6 nM for AKT2). CCT128930 has 28-fold selectivity over the closely related PKA kinase (IC $_{50}$ =168 nM) through the targeting of Met282 of AKT (Met173 of PKA-AKT chimera), as well as 20-fold selectivity over p70S6K (IC $_{50}$ =120 nM). Antitumor activity.			
IC <sub>50</sub> & Target	Akt2 6 nM (IC <sub>50</sub> ) Apoptosis	p70S6K 120 nM (IC <sub>50</sub> )	PKA 168 nM (IC <sub>50</sub> )	Autophagy

#### In Vitro

The  $GI_{50}$  values of CCT128930 for growth inhibition are 6.3  $\mu$ M for U87MG human glioblastoma cells, 0.35  $\mu$ M for LNCaP human prostate cancer cells, and 1.9  $\mu$ M for PC3 human prostate cancer cells, all of which are PTEN-deficient human tumor cell lines<sup>[1]</sup>.

CCT128930 (0.1-60  $\mu$ M; 1 hour; U87MG human glioblastoma cells) shows an initial induction of AKT phosphorylation at serine 473 up to 20  $\mu$ M, followed by a decreased in phosphorylation at higher concentrations<sup>[1]</sup>.

CCT128930 inhibits direct substrates of AKT (Ser9 GSK3 $\beta$ , pThr246 PRAS40 and pT24 FOXO1/p32 FOXO3a) at  $\geq$ 5  $\mu$ M, and the downstream target, pSer235/236 S6RP at  $\geq$  10  $\mu$ M, with generally constant levels of the respective total proteins and GAPDH [1].

CCT128930 (18.9  $\mu$ M; U87MG human glioblastoma cells) causes an increase in phosphorylation of pSer473 AKT after 30 minutes, which is sustained for 48 hours. Total AKT protein signal decreases gradually from 8 hours to 48 hours of treatment [1]

CCT128930 (PTEN-null U87MG human glioblastoma cells; over a 24-hour time period) results in an increase in G0/G1 phase cells from 43.6% to 64.8% after 24 hours of treatment<sup>[1]</sup>.

CCT128930 (0-10  $\mu$ M; 24 hours) increases, but not inhibites, the phosphorylation of Akt in HepG2 and A549 cells. CCT128930 (0-20  $\mu$ M; 24 hours) inhibits cell proliferation by inducing cell cycle arrest in G1 phase through downregulation of cyclinD1 and Cdc25A, and upregulation of p21, p27 and p53. CCT128930 (20  $\mu$ M) triggers cell apoptosis with activation of caspase-3, caspase-9, and PARP. CCT128930 (0-20  $\mu$ M; 24 hours) increases phosphorylation of ERK and JNK in HepG2 cells. CCT128930 (0-20  $\mu$ M; 24 hours) activates DNA damage response of HepG2 cell characterized by phosphorylation of H2AX, ATM (ataxiatelangiectasia mutated), Chk1 and Chk2<sup>[2]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

### In Vivo

CCT128930 (25 or 40 mg/kg; i.p. daily or twice daily for 5 days) shows antitumor activities in U87MG and BT474 human breast cancer xenografts  $^{[1]}$ .

Summary of the pharmacokinetic parameters of CCT128930 (25 mg/kg) in CrTacNCr-Fox1nu mice<sup>[1]</sup>

Tissue	Route	T <sub>1/2</sub> (h)	T <sub>max</sub> (h)	C <sub>max</sub> (μM)	V <sub>ss</sub> (L)	Cl (L/h)	AUC <sub>0-∞</sub> (μMh)	Bioavailability (%)
Plasma	i.v.	0.95	0.083	6.36	0.25	0.325	4.62	100
Plasma	i.p.	2.33	0.5	1.28	N/A	0.372	1.33	28.8
Tumor	i.p.	3.89	1	8.02	N/A	0.06*	25.8	N/A
Plasma	p.o.	0.57	0.5	0.432	N/A	0.317	0.392	8.5

#### \*Apparent clearance.

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Animal Model:	6-8 weeks old female CrTacNCr-Fox1nu mice $^{[1]}$		
Dosage:	25 mg/kg (U87MG human glioblastoma xenografts) or 40 mg/kg (BT474 human breast cancer xenografts)		
Administration:	i.p. daily for 5 days (U87MG human glioblastoma xenografts); i.p. twice daily for 5 days (BT474 human breast cancer xenografts)		
Result:	Giving a treated:control (T/C) ratio on day 12 of 48%. There was no weight loss associated with this regime in U87MG human glioblastoma xenografts.  Had a profound antitumor effect with complete growth arrest and a T/C ratio of 29% on day 22. This regimen was associated with minimal weight loss, with a nadir of only 94.8%		

of the initial body weight on day 15 of treatment in BT474 human breast cancer xenografts.

## **CUSTOMER VALIDATION**

- Biochem Biophys Res Commun. 2021 May 11;560:132-138.
- J Healthc Eng. 05 Jan 2022.
- Oncotarget. 2016 May 17;7(20):29131-42.

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#### **REFERENCES**

[1]. Yap TA et al. Preclinical pharmacology, antitumor activity, and development of pharmacodynamic markers for the novel, potent AKT inhibitor CCT128930. Mol Cancer Ther. 2011 Feb;10(2):360-71.

[2]. Wang FZ, et al. CCT128930 induces cell cycle arrest, DNA damage, and autophagy independent of Akt inhibition. Biochimie. 2014;103:118-125.

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

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