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产品名称：CC-115 (hydrochloride)
产品别名：CC-115 hydrochloride

生物活性：

Description	CC-115 hydrochloride is a potent and dual DNA-PK and mTOR kinase inhibitor with IC_{50}s of 13 nM and 21 nM, respectively. CC-115 blocks both mTORC1 and mTORC2 signaling.

IC_{50} & Target	mTOR	mTORC1	mTORC2	DNA-PK	PI3Kα
	21 nM (IC_{50})			13 nM (IC_{50})	852 nM (IC_{50})

In Vitro	CC-115 inhibits PC-3 cells proliferation with an IC_{50} of 138 nM. In a kinase selectivity assessment against a panel of 250 protein kinases at 3 μM, only one kinase other than mTOR kinase is identified with more than 50% inhibition (cFMS 57%, IC_{50}=2.0 μM). Of the PI3K related kinases (PIKKs) tested, CC-115 proves to be equipotent against DNA PK (IC_{50}=15 nM) and demonstrates 40 to >1000 fold selectivity against the remaining PIKKs tested; PI3K-alpha (IC_{50}=0.85 μM), ATR (50% inhibition at 30 μM) and ATM (IC_{50}>30 μM). The IC_{50} values for CC-115 are >10 μM against a panel of CYP enzymes and >33 μM for the hERG (human ether-a-go-go-related gene) ion channel. When screened in a single point assay at 10 μM against a Cerep receptor and enzyme panel only one target is inhibited >50% (PDE3, IC_{50}=0.63 μM)[1].
In Vivo	CC-115 hydrochloride shows good in vivo PK profiles across multiple species with 53%, 76% and ~100% oral bioavailability in mouse, rat and dog, respectively. CC-115 is tested at lower doses of 0.25, 0.5 and 1 mg/kg bid or 1 mg/kg qd, with observed corresponding tumor volume reductions of 46%, 57%, 66% and 57% respectively. CC-115 sustains inhibition though 24 hours. At the 1 mg/kg dose CC-115 shows significant inhibition at 1 and 3 hours, CC-115 demonstrating inhibition through 10 hours. CC-115 is evaluated using both once (qd) and twice (bid) daily dosing schedules[1].

Solvent&Solubility

In Vitro:

DMSO : ≥ 30 mg/mL (80.47 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6823 mL	13.4117 mL	26.8233 mL
	5 mM	0.5365 mL	2.6823 mL	5.3647 mL
	10 mM	0.2682 mL	1.3412 mL	2.6823 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

References	[1]. Mortensen DS, et al. Optimization of a Series of Triazole Containing Mammalian Target of Rapamycin (mTOR) Kinase Inhibitors and the Discovery of CC-115. J Med Chem. 2015 Jul 23;58(14):5599-5608.

实验参考：

Cell Assay	PC-3 cells are cultured in growth media. For biomarker studies cells are treated for 1 h and then assayed for pS6 and pAkt levels using MesoScale technology. For proliferation experiments, cells are treated with compound (e.g., CC-115) and then allowed to grow for 72 h. All data are normalized

	and represented as a percentage of the DMSO-treated cells. Results are then expressed as IC_{50} values[1].
Animal Administration	Mice[1] Encouraged by the observed exposures, CC-115 is advanced into single dose PK/PD studies assessing mTOR pathway biomarker inhibition in tumor bearing mice. PC-3 tumor-bearing mice are administered with a single dose of CC-115, dosed orally at either 1 or 10 mg/kg, and plasma and tumor samples are collected at various time points for analysis. Significant inhibition of both mTORC1 (pS6) and mTORC2 (pAktS473) is observed for all compounds and the level of biomarker inhibition correlated to plasma compound levels.
Kinase Assay	An HTR-FRET substrate phosphorylation assay is employed for mTOR kinase. PI3Kα IC_{50} determinations are outsourced using the mobility shift assay format. Compounds (e.g., CC-115) are assessed against concentrations of ATP at approximately the Km for the assay, with average ATP Km of 15 μM and 50 μM for the mTOR and PI3K assays, respectively[1].
References	[1]. Mortensen DS, et al. Optimization of a Series of Triazole Containing Mammalian Target of Rapamycin (mTOR) Kinase Inhibitors and the Discovery of CC-115. J Med Chem. 2015 Jul 23;58(14):5599-5608.