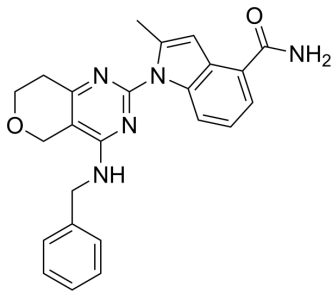
CB-5083

Cat. No.:	HY-12861
CAS No.:	1542705-92-9
Molecular Formula:	$C_{24}H_{23}N_5O_2$
Molecular Weight:	413
Target:	p97
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 : 100 mg/mL (242.13 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4213 mL	12.1065 mL	24.2131 mL
	5 mM	0.4843 mL	2.4213 mL	4.8426 mL
	10 mM	0.2421 mL	1.2107 mL	2.4213 mL

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

In Vivo

1. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 10 mg/mL (24.21 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.05 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.05 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.05 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CB-5083 is a first-in-class, potent, selective, and orally bioavailable inhibitor of the p97 AAA ATPase/VCP. CB-5083 selectively inhibits p97 through its D2 site with the IC_{50} of 11 nM[1].

IC_{50} & Target

IC50: 11 nM (p97)[1]

In Vitro	CB-5083 shows cell killing potency with IC_{50}s of 0.68, 0.68, 1.03, and 0.49 μM for lung carcinoma A549 CTG, A549 K48, A549 CHOP, and A549 p62, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	CB-5083 (75 mg/kg; oral administration; qd; for 2 weeks) shows antitumor activity in an HCT 116 tumor xenograft model[1]. CB-5083 exhibits terminal elimination half-life ($T_{1/2}$=2.56 h), moderate oral bioavailability (mouse 41%) and C_{max} (mouse 7.95 μM) following oral administration (25 mg/kg) in female nude mice[1]. CB-5083 exhibits terminal elimination half-life ($T_{1/2}$=2.83 h) due to high plasma clearance (5.9 mL/min/kg respectively) combined with large volumes of distribution (418 mL/kg respectively) following intravenous administration (3.0 mg/kg) in female nude mice[1]. CB-5083 has good metabolic stability with a 102 min $T_{1/2}$ in a mouse liver microsomal stability study and a 172 min $T_{1/2}$ in a hepatocyte stability study[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Nu/Nu nude female mice bearing established human tumor xenografts derived from HCT 116 colon[1]
Dosage:	75 mg/kg
Administration:	Administered orally using every day (qd) dosing, for 2 weeks.
Result:	Showed more profound antitumor activity.

CUSTOMER VALIDATION

- Cell. 2020 Dec 10;183(6):1714-1731.e10.
- Nat Chem Biol. 2023 Aug 31.
- Sci Adv. 2021 May 14;7(20):eabg2099.
- Leukemia. 2019 Jul;33(7):1675-1686.
- Cell Rep. 2021 May 25;35(8):109153.

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REFERENCES

[1]. Zhou HJ, et al. Discovery of a First-in-Class, Potent, Selective, and Orally Bioavailable Inhibitor of the p97 AAA ATPase (CB-5083). J Med Chem. 2015 Dec 24;58(24):9480-97.

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