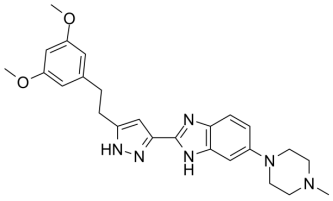
CPL304110

Cat. No.:	HY-131908
CAS No.:	1627826-19-0
Molecular Formula:	$C_{25}H_{30}N_6O_2$
Molecular Weight:	446.54
Target:	FGFR
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (223.94 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2394 mL	11.1972 mL	22.3944 mL
	5 mM	0.4479 mL	2.2394 mL	4.4789 mL
	10 mM	0.2239 mL	1.1197 mL	2.2394 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: ≥ 2.5 mg/mL (5.60 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.60 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.60 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CPL304110 is a potent, orally active and selective inhibitor of fibroblast growth factor receptors FGFR (1-3), with IC_{50} values of 0.75 nM, 0.5 nM, and 3.05 nM for FGFR (1-3), respectively[1].

IC_{50} & Target			
	FGFR1 0.75 nM (IC_{50})	FGFR2 0.5 nM (IC_{50})	FGFR3 3.05 nM (IC_{50})

In Vitro

CPL304110 (0-0.6 μM) dose-dependently inhibits FGFR2 phosphorylation and downstream signaling (p-ERK)[1].
CPL304110 (compound 56q) exhibits in SNU-16 proliferation assay with an IC_{50} of 85.64 nM[1].

CPL304110 (compound 56q) demonstrats a more than 45-fold, 345-fold, 395-fold and 680-fold selectivity over KDR (VEGFR2), Flt3, Aura A and PDGFRb, respectively relative to FGFR2, and no significant inhibitory effects were observed with other tyrosine kinases[1].

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

Western Blot Analysis[1]

Cell Line:	SNU-16 cell lines.
Concentration:	0-0.6 μM.
Incubation Time:	1 h.
Result:	Suppressed FGFR2 phosphorylation and downstream signaling (p-ERK)

In Vivo

CPL304110 (p.o., 40 mg/kg) exhibits a $t_{1/2}$ of 2 h and C_{max} of 3369 ng/mL in mice[1].

CPL304110 (compound 56q, 2 X 20 mg/kg) significantly inhibits tumor growth in mice without significant body loss or any toxicity. On day 21 (D21, day of termination) the tumor growth inhibition (TGI) is 64% for dosing 20 mg/kg twice a day[1].

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

Animal Model:	Severe combined immunodeficient (SCID) mice implanted subcutaneously with SNU-16 (human)[1].
Dosage:	20 mg/kg (X2).
Administration:	Orally, twice daily for 21 days.
Result:	After 6 hours of last dosing, concentration of 56q decreased in the plasma (9%) but increased stepwise in the tumor cells (121%).

REFERENCES

[1]. Abdellah Yamani, et al. Discovery and optimization of novel pyrazole-benzimidazole CPL304110, as a potent and selective inhibitor of fibroblast growth factor receptors FGFR (1-3). Eur J Med Chem. 2020 Nov 7;112990.

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