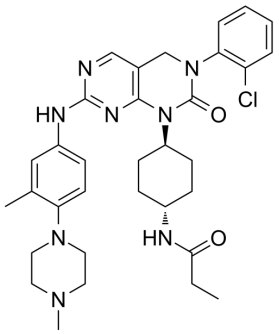
JND3229

Cat. No.:	HY-119944
CAS No.:	2260886-64-2
Molecular Formula:	$C_{33}H_{41}ClN_8O_2$
Molecular Weight:	617.18
Target:	EGFR
Pathway:	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 12.5 mg/mL (20.25 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6203 mL	8.1014 mL	16.2027 mL
	5 mM	0.3241 mL	1.6203 mL	3.2405 mL
	10 mM	0.1620 mL	0.8101 mL	1.6203 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: ≥ 1.25 mg/mL (2.03 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.25 mg/mL (2.03 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (2.03 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

JND3229 is a reversible $EGFR^{C797S}$ inhibitor with IC_{50} values of 5.8, 6.8 and 30.5 nM for $EGFR^{L858R/T790M/C797S}$, $EGFR^{WT}$ and $EGFR^{L858R/T790M}$, respectively. JND3229 has good anti-proliferative activity and can effectively inhibit tumour growth in vivo. JND3229 can be used in cancer research, especially in non-small cell carcinoma[1].

IC_{50} & Target

IC50: 5.8 nM ($EGFR^{L858R/T790M/C797S}$), 6.8 nM ($EGFR^{WT}$), 30.5 nM ($EGFR^{L858R/T790M}$)[1].

In Vitro

JND3229 potently inhibits the proliferation of BaF3 cells (harboring the $EGFR^{L858R/T790M/C797S}$ and $EGFR^{19D/T790M/C797S}$

mutations), NCI-H1975 NSCLC cells (with $EGFR^{T790M}$ mutation) and A431 cancer cells (overexpressing $EGFR^{WT}$) with IC_{50} values of 0.51, 0.32, 0.31 and 0.27 μM, respectively[1].
JND3229 (0.1, 0.3, 1, 3, 10 μM; 2 h) potently inhibits the phosphorylation of $EGFR^{L858R/T790M/C797S}$ and $EGFR^{19D/T790M/C797S}$ in engineering BaF3 cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	BaF3 cells (overexpressing $EGFR^{L858R/T790M/C797S}$ or $EGFR^{19D/T790M/C797S}$)
Concentration:	0.1, 0.3, 1, 3, 10 μM
Incubation Time:	2 h
Result:	Significantly inhibited the phosphorylation of $EGFR^{L858R/T790M/C797S}$ and EGFR $^{19D/T790M/C797S}$ in a dose-dependent manner.

In Vivo

JND3229 (10 mg/kg; i.p.; twice daily for 10 days) exhibits an obvious suppression of tumor growth, and shows target inhibition in vivo[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	BALB/c mice (bearing established BaF3-EGFR19D/T790M/C797S mouse xenograft tumors model)[1].
Dosage:	10 mg/kg
Administration:	Intraperitoneal injection; twice daily for 10 days.
Result:	Caused an obvious suppression of tumor growth with a Tumor Growth Inhibition (TGI) value of 42.2%. Showed well tolerance without obvious body weight loss or other obvious toxic sign in the treated animals. Significantly decreased the level of phosphorylated EGFR (p-EGFR) tin the tumor tissues.

REFERENCES

[1]. Lu X, et al. Discovery of JND3229 as a New EGFRC797S Mutant Inhibitor with In Vivo Monodrug Efficacy. ACS Med Chem Lett. 2018 Oct 8;9(11):1123-1127.

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

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