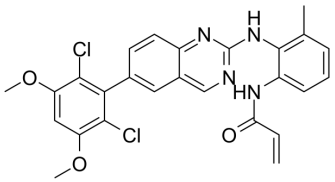
BLU9931

Cat. No.:	HY-12823
CAS No.:	1538604-68-0
Molecular Formula:	$C_{26}H_{22}Cl_2N_4O_3$
Molecular Weight:	509.38
Target:	FGFR
Pathway:	Protein Tyrosine Kinase/RTK
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 : 83.33 mg/mL (163.59 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9632 mL	9.8159 mL	19.6317 mL
	5 mM	0.3926 mL	1.9632 mL	3.9263 mL
	10 mM	0.1963 mL	0.9816 mL	1.9632 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 (4.08 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.08 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.08 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BLU9931 is a potent, highly selective, and irreversible fibroblast growth factor receptor 4 (FGFR4) inhibitor with an IC_{50} of 3 nM and a K_d of 6 nM. BLU9931 has significant antitumor activity[1].

IC_{50} & Target	FGFR1	FGFR2	FGFR3	FGFR4
	591 nM (IC_{50})	493 nM (IC_{50})	150 nM (IC_{50})	3 nM (IC_{50})

In Vitro

BLU9931 inhibits proliferation of HCC cell lines that express an intact FGFR4 signaling complex, with EC_{50}s of 0.07 μM, 0.11 μ

M and 0.02 μM for Hep 3B, HuH7 and JHH7 cells, respectively[1].

BLU9931 (0.3-300 nM; 1 hour; MDA-MB-453 and Hep 3B cells) treatment demonstrates potent, dose-dependent reduction of phosphorylation of FGFR4 signaling pathway components, including fibroblast growth factor receptor substrate 2 (FRS2), MAPK, and AKT in MDA-MB-453 cells. BLU9931 shows dose-dependent inhibition of the signaling cascade downstream of FGFR4. BLU9931 exhibits potent inhibition of phosphorylation of the FGFR4 pathway components in Hep 3B cells. BLU9931 treatment leads to induction of caspase-3/7 activity, indicative of induction of apoptosis that results in inhibition of signaling downstream of FGFR4[1].

BLU9931 (100 nM; 0 -24 hours; Hep 3B cells) treatment increases CYP7A1 mRNA expression and the expression of the proliferative marker EGR1 is inhibited[1].

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

Western Blot Analysis[1]

Cell Line:	MDA-MB-453 and Hep 3B cells
Concentration:	0.3 nM, 1 nM, 3 nM, 10 nM, 30 nM, 100 nM, 300 nM
Incubation Time:	1 hour
Result:	Demonstrated potent, dose-dependent reduction of phosphorylation of FGFR4 signaling pathway components, including fibroblast growth factor receptor substrate 2 (FRS2), MAPK, and AKT in MDA-MB-453 and Hep 3B cells.

RT-PCR[1]

Cell Line:	Hep 3B cells
Concentration:	100 nM
Incubation Time:	0 hour, 4 hours, 8 hour, 24 hours
Result:	Increased CYP7A1 mRNA expression. And the expression of the proliferative marker EGR1 was inhibited.

In Vivo

BLU9931 (10-100 mg/kg; oral administration; twice every day; for 21 days; mice) treatment demonstrates antitumor activity in HCC xenograft models[1].

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

Animal Model:	Mice injected with Hep 3B cells[1]
Dosage:	10 mg/kg, 30 mg/kg or 100 mg/kg
Administration:	Oral administration; twice every day; for 21 days
Result:	Resulted in dose-dependent growth inhibition of Hep 3B tumors. Prevented weight loss in a dose-dependent manner.

CUSTOMER VALIDATION

- Theranostics. 2021 Mar 5;11(10):5045-5060.
- Clin Transl Med. 2022 Nov;12(11):e1102.
- Int J Biol Sci. 2021 Jun 22;17(10):2576-2589.
- Int J Biol Sci. 2021; 17(10): 2576-2589.

- Eur J Med Chem. 2023 Nov 5, 259, 115703.

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REFERENCES

[1]. Hagel M, et al. First Selective Small Molecule Inhibitor of FGFR4 for the Treatment of Hepatocellular Carcinomas with an Activated FGFR4 Signaling Pathway. Cancer Discov. 2015 Apr;5(4):424-37.

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