产品名称：**BLU9931**
产品别名：**BLU9931**

生物活性：				
Description	BLU9931 is a potent, highly selective, and irreversible fibroblast growth factor receptor 4 (FGFR4) inhibitor with an IC50 of 3 nM and a Kd 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 EC50s of 0.07 μM, 0.11 μM 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].			
	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].			
	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.		
	In Vitro: **DMSO : 17 mg/mL (33.37 mM; Need ultrasonic and warming)** **H2O : < 0.1 mg/mL (insoluble)**			

Solvent&Solubility

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

*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。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (4.91 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.91 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)

Solubility: 2.5 mg/mL (4.91 mM); Suspended solution; Need ultrasonic

此方案可获得 2.5 mg/mL (4.91 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。

3.请依序添加每种溶剂： 10% DMSO →90% corn oil

Solubility: ≥ 2.5 mg/mL (4.91 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.91 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。

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.