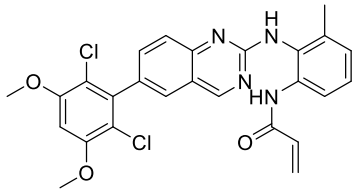
Product data sheet

MedKoo Cat#: 206192 Name: BLU9931 CAS#: 1538604-68-0 Chemical Formula: $C_{26}H_{22}Cl_2N_4O_3$ Exact Mass: 508.1069 Molecular Weight: 509.38	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

BLU9931 is a potent and irreversible small-molecule inhibitor of FGFR4, as a targeted therapy to treat patients with HCC whose tumors have an activated FGFR4 signaling pathway. BLU9931 is exquisitely selective for FGFR4 versus other FGFR family members and all other kinases. BLU9931 shows remarkable antitumor activity in mice bearing an HCC tumor xenograft that overexpresses FGF19 due to amplification as well as a liver tumor xenograft that overexpresses FGF19 mRNA but lacks FGF19 amplification. Approximately one third of patients with HCC whose tumors express FGF19 together with FGFR4 and its coreceptor klotho β (KLB) could potentially respond to treatment with an FGFR4 inhibitor.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	67.78	133.06

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.96 mL	9.82 mL	19.63 mL
5 mM	0.39 mL	1.96 mL	3.93 mL
10 mM	0.20 mL	0.98 mL	1.96 mL
50 mM	0.04 mL	0.20 mL	0.39 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Sasaki N, Gomi F, Yoshimura H, Yamamoto M, Matsuda Y, Michishita M, Hatakeyama H, Kawano Y, Toyoda M, Korc M, Ishiwata T. FGFR4 Inhibitor BLU9931 Attenuates Pancreatic Cancer Cell Proliferation and Invasion While Inducing Senescence: Evidence for Senolytic Therapy Potential in Pancreatic Cancer. Cancers (Basel). 2020 Oct 14;12(10):2976. doi: 10.3390/cancers12102976. PMID: 33066597; PMCID: PMC7602396.
2. Hagel M, Miduturu C, Sheets M, Rubin N, Weng W, Stransky N, Bifulco N, Kim JL, Hodous B, Brooijmans N, Shutes A, Winter C, Lengauer C, Kohl NE, Guzi T. 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. doi: 10.1158/2159-8290.CD-14-1029. Epub 2015 Mar 16. PMID: 25776529.

In vivo study

1. Yamamoto M, Nomura S, Hosoi A, Nagaoka K, Iino T, Yasuda T, Saito T, Matsushita H, Uchida E, Seto Y, Goldenring JR, Kakimi K, Tatematsu M, Tsukamoto T. Established gastric cancer cell lines transplantable into C57BL/6 mice show fibroblast growth

factor receptor 4 promotion of tumor growth. Cancer Sci. 2018 May;109(5):1480-1492. doi: 10.1111/cas.13569. Epub 2018 Apr 15. PMID: 29532565; PMCID: PMC5980194.
2. Hagel M, Miduturu C, Sheets M, Rubin N, Weng W, Stransky N, Bifulco N, Kim JL, Hodous B, Brooijmans N, Shutes A, Winter C, Lengauer C, Kohl NE, Guzi T. 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. doi: 10.1158/2159-8290.CD-14-1029. Epub 2015 Mar 16. PMID: 25776529.

7. Bioactivity

Biological target:

BLU9931 is an irreversible fibroblast growth factor receptor 4 (FGFR4) inhibitor with an IC50 of 3 nM and a Kd of 6 nM.

In vitro activity

PK-1 cells exhibited a dose-dependent decrease in proliferation in the presence of BLU9931 (Figure 3A). An inhibitory effect on proliferation was also observed in T3M-4 cells (Figure S3A). By contrast, BLU9931 did no inhibit proliferation in PK-45P cells (Figure 3A), which expressed very low FGFR4 levels (Figure 1). Next, this study examined whether BLU9931 exerts toxic effects in PDAC cells. Incubation of PK-1 cells with 2 μM BLU9931 followed by fluorescence activated cell sorter (FACS) analysis using annexin V and propidium iodide (PI) showed that ~2% of the cells underwent apoptosis, necrosis, or cell injury (Figure 3B). Higher concentration (>10 μM) of BLU9931 revealed dead and floating cells suggestive of a toxic effect at these very high concentrations of the drug.

Reference: Cancers (Basel). 2020 Oct; 12(10): 2976. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7602396/

In vivo activity

Mice with YTN16 s.c. transplanted or peritoneally transplanted mice were treated for 3 weeks with BLU9931, a potent, selective, and irreversible FGFR4 inhibitor. Growth of s.c. tumor in BLU9931-treated mice was slightly blunted compared to non-treated mice (Figure 7A,B). However, the growth of peritoneal dissemination was remarkably different. Only very small spots of peritoneal dissemination were detected macroscopically and microscopically in BLU9931-treated mice (Figure 7C,D,E,G). Surprisingly, the histology of s.c. tumor after BLU9931 treatment was remarkably different from that of the original tumor, even though the difference in growth rate was small (Figure 7F,H). YTN16 tumor formed glands, whereas BLU9931-treated YTN16 tumor formed few glands in all 3 transplanted mice. After activation of FGFR, signaling of Stat3, Erk, and Akt is known to be activated downstream. Staining for all 3 markers was weaker in BLU9931-treated tumor compared to the original YTN16 tumor.

Reference: Cancer Sci. 2018 May; 109(5): 1480–1492. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5980194/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.