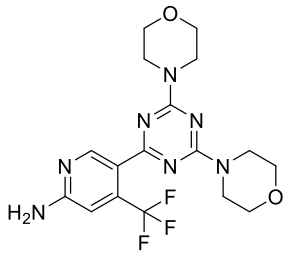
Product data sheet

MedKoo Cat#: 206146 Name: Bimiralisib free base CAS#: 1225037-39-7 (free base) Chemical Formula: $C_{17}H_{20}F_3N_7O_2$ Exact Mass: 411.1631 Molecular Weight: 411.3892	
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:
Bimiralisib, also known as PQR309, is an orally bioavailable pan inhibitor of phosphoinositide-3-kinases (PI3K) and inhibitor of the mammalian target of rapamycin (mTOR), with potential antineoplastic activity. PI3K/mTOR kinase inhibitor PQR309 inhibits the PI3K kinase isoforms alpha, beta, gamma and delta and, to a lesser extent, mTOR kinase, which may result in tumor cell apoptosis and growth inhibition in cells overexpressing PI3K/mTOR. Activation of the PI3K/mTOR pathway promotes cell growth, survival, and resistance to both chemotherapy and radiotherapy.

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	22.0	53.48
DMF	10.0	24.31
Ethanol	2.0	4.86

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.43 mL	12.15 mL	24.31 mL
5 mM	0.49 mL	2.43 mL	4.86 mL
10 mM	0.24 mL	1.22 mL	2.43 mL
50 mM	0.05 mL	0.24 mL	0.49 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. Yang K, Tang XJ, Xu FF, Liu JH, Tan YQ, Gao L, Sun Q, Ding X, Liu BH, Chen QX. PI3K/mTORC1/2 inhibitor PQR309 inhibits proliferation and induces apoptosis in human glioblastoma cells. Oncol Rep. 2020 Mar;43(3):773-782. doi: 10.3892/or.2020.7472. Epub 2020 Jan 20. PMID: 32020210; PMCID: PMC7040887.
2. Tarantelli C, Gaudio E, Arribas AJ, Kwee I, Hillmann P, Rinaldi A, Cascione L, Spriano F, Bernasconi E, Guidetti F, Carrassa L, Pittau RB, Beaufils F, Ritschard R, Rageot D, Sele A, Dossena B, Rossi FM, Zucchetto A, Taborelli M, Gattei V, Rossi D, Stathis A, Stussi G, Broggini M, Wymann MP, Wicki A, Zucca E, Cmiljanovic V, Fabbro D, Bertoni F. PQR309 Is a Novel Dual PI3K/mTOR Inhibitor with Preclinical Antitumor Activity in Lymphomas as a Single Agent and in Combination Therapy. Clin Cancer Res. 2018 Jan 1;24(1):120-129. doi: 10.1158/1078-0432.CCR-17-1041. Epub 2017 Oct 24. PMID: 29066507.

In vivo study

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1. von Achenbach C, Weller M, Kaulich K, Gramatzki D, Zacher A, Fabbro D, Reifenberger G, Szabó E. Synergistic growth inhibition mediated by dual PI3K/mTOR pathway targeting and genetic or direct pharmacological AKT inhibition in human glioblastoma models. J Neurochem. 2020 May;153(4):510-524. doi: 10.1111/jnc.14899. Epub 2020 Jan 8. PMID: 31618458.
2. Beaufils F, Cmiljanovic N, Cmiljanovic V, Bohnacker T, Melone A, Marone R, Jackson E, Zhang X, Sele A, Borsari C, Mestan J, Hebeisen P, Hillmann P, Giese B, Zvelebil M, Fabbro D, Williams RL, Rageot D, Wymann MP. 5-(4,6-Dimorpholino-1,3,5-triazin-2-yl)-4-(trifluoromethyl)pyridin-2-amine (PQR309), a Potent, Brain-Penetrant, Orally Bioavailable, Pan-Class I PI3K/mTOR Inhibitor as Clinical Candidate in Oncology. J Med Chem. 2017 Sep 14;60(17):7524-7538. doi: 10.1021/acs.jmedchem.7b00930. Epub 2017 Sep 1. PMID: 28829592; PMCID: PMC5656176.

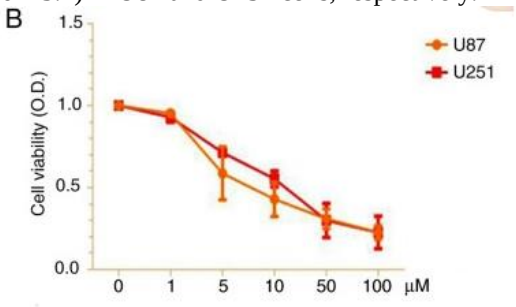
7. Bioactivity

Biological target:

Bimiralisib (PQR309) is a brain-penetrant, pan-class I PI3K/mTOR inhibitor with IC50s of 33 nM, 451 nM, 661 nM, 708 nM and 89 nM for PI3Kα, PI3Kδ, PI3Kβ, PI3Kγ and mTOR, respectively.

In vitro activity

The results of a CCK-8 assay revealed a significant suppressive effect of PQR309 on U87 and U251 cells. The results indicated that the viability of the cells was significantly ($P<0.05$) suppressed in a dose- and time-dependent manner after the cells were treated with PQR309 (0, 1, 5, 10, 50 and 100 µM) after 72 h (Fig. 1B). The colony formation rates of treated U87 and U251 cells decreased in various concentration groups compared to the control (Fig. 1C-D). According to these results, the IC50 values of PQR309 were 7.104 (95% CI, 5.6–8.5) and 11.986 (95% CI, 10.6–13.4) in U87 and U251 cells, respectively.



Reference: Oncol Rep. 2020 Mar; 43(3): 773–782. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7040887/

In vivo activity

Rats were injected with 2 × 107 human PC3 prostate cancer cells into one flank and randomized after 16 days. From day 17 the control group received vehicle once daily. Compound 1 (bimiralisib) was orally administered at 5 mg/kg, 10 mg/kg (both daily, QD), or 15 mg/kg [5 consecutive days, 2 days off drug (QD × 5, 2 days off)] for 28 days to match the timelines of regulatory toxicology studies. Treatment with 1 led to significant tumor size reductions: tumor growth was inhibited dose-dependently (best T/C of 31–12%, Figure 6A). Compound 1 was best tolerated at 5 mg/kg without significant body weight changes (Figure 6B). At 10 mg/kg, 1 caused a reduction of body weight, which accumulated to a reduction of 15% after 28 days of treatment. Similarly, 15 mg/kg of 1 led to body weight loss after 5 days of treatment, which was reversible during the recovery period. After 28 days of drug exposure (day 44 of the experiment), animals with body weight loss fully recovered within a treatment-free period (days 45–50) without overt signs of tumor cell proliferation. In a subsequent treatment period tumor growth remained inhibited and body weight loss was only observed in the 15 mg/kg group.

Reference: J Med Chem. 2017 Sep 14; 60(17): 7524–7538. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5656176/

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.