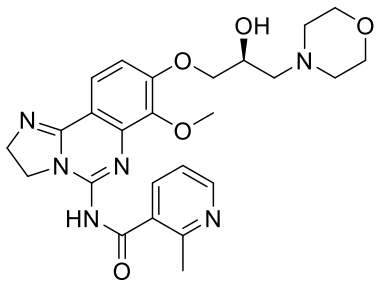
Product data sheet

MedKoo Cat#: 205923 Name: BAY1082439 CAS#: 1375469-38-7 Chemical Formula: $C_{25}H_{30}N_6O_5$ Exact Mass: 494.2278 Molecular Weight: 494.552	
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:

BAY1082439 is an orally bioavailable inhibitor of the class I phosphoinositide 3-kinase (PI3K) alpha and beta isoforms with potential antineoplastic activity. PI3K alpha/beta inhibitor BAY1082439 selectively inhibits both PI3K alpha, including mutated forms of PIK3CA, and PI3K beta in the PI3K/Akt/mTOR pathway, which may result in tumor cell apoptosis and growth inhibition in PI3K-expressing and/or PTEN-driven tumor cells. By specifically targeting class I PI3K alpha and beta, this agent may be more efficacious and less toxic than pan PI3K inhibitors.

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	5	10.11

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.02 mL	10.11 mL	20.22 mL
5 mM	0.40 mL	2.02 mL	4.04 mL
10 mM	0.20 mL	1.01 mL	2.02 mL
50 mM	0.04 mL	0.20 mL	0.40 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. Zou Y, Qi Z, Guo W, Zhang L, Ruscetti M, Shenoy T, Liu N, Wu H. Cotargeting the Cell-Intrinsic and Microenvironment Pathways of Prostate Cancer by PI3Kα/β/δ Inhibitor BAY1082439. Mol Cancer Ther. 2018 Oct;17(10):2091-2099. doi: 10.1158/1535-7163.MCT-18-0038. Epub 2018 Jul 25. PMID: 30045927; PMCID: PMC6168338.

In vivo study

1. Zou Y, Qi Z, Guo W, Zhang L, Ruscetti M, Shenoy T, Liu N, Wu H. Cotargeting the Cell-Intrinsic and Microenvironment Pathways of Prostate Cancer by PI3Kα/β/δ Inhibitor BAY1082439. Mol Cancer Ther. 2018 Oct;17(10):2091-2099. doi: 10.1158/1535-7163.MCT-18-0038. Epub 2018 Jul 25. PMID: 30045927; PMCID: PMC6168338.

7. Bioactivity

Biological target:

BAY1082439 is an orally bioavailable, selective PI3Kα/β/δ inhibitor.

In vitro activity

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To test whether BAY1082439 (Fig. S1A) could achieve better efficacy by preventing rebound activation of the PI3K pathway, PC3 and LNCaP cells, both PTEN-null human prostate cancer cell lines, were treated with various concentrations of BAY1082439 for 72 hours. BAY1082439 effectively inhibited cell growth (Fig. 1A) by blocking the G1/S cell cycle transition and by inducing apoptosis (Fig. S1B-C). The PI3Kβ-specific inhibitor TGX-221 and the PI3Kα-specific inhibitor BYL-719 were significantly less effective in inhibiting cell growth and blocking the G1 to S transition (Fig. 1A; Fig. S1C). In isogenic PC3 PTEN-WT and PTEN-null cells, PTEN-null cells were three orders of magnitude more sensitive to BAY1082439 than WT cells (Fig. 1B), indicating a wide, PTEN status-dependent therapeutic window. In both human prostate cancer cell lines and the CaP8 and CaP2 cell lines derived from the CP mice, BAY1082439 prevented the feedback activation of the PI3K pathway and the rebound AKT phosphorylation seen with TGX-221 treatment (Fig. 1C and Fig. 1D), and demonstrated equal potency to inhibit cell growth as the combination of the PI3Kα and PI3Kβ inhibitors TGX-221 and BYL-719 (Fig. 1E).

Reference: Mol Cancer Ther. 2018 Oct;17(10):2091-2099. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/30045927/

In vivo activity

Based on the superior and sustainable activity of BAY1082439 to inhibit AKT phosphorylation of human and mouse PTEN-null prostate cancer lines (Fig. 1C-D), the effect of BAY1082439 was tested in vivo. CP mice were treated with 75 mg/kg of BAY1082439 daily, starting at 6 weeks when PINs form, and ending at 10 weeks when untreated tumors progress to localized adenocarcinoma (Fig. 2A). BAY1082439 was well tolerated over the course of the study (Fig. S2). In comparison to the vehicle controls, the BAY1082439 treatment group showed significantly decreased tumor size and P-AKT staining, nearly normal luminal architecture (Fig. 2B; Fig. S3A), and a significant reduction of Ki67-positive cells (Fig. 2C). Smooth muscle actin (SMA) staining indicated no local invasion in the BAY1082439 treatment group compared to vehicle controls (Fig. S3B). We also tested the effect of BAY1082439 on PC3 xenograft tumors in vivo, which harbors PTEN and P53 mutations. BAY1082439 can significantly inhibit the human prostate cancer growth as compared to vehicle controls (Fig. 2D). Together, these results showed that BAY1082439 effectively prevented prostate cancer progression in the clinically relevant CP model and inhibit aggressive human prostate cancer cell growth in vivo.

Reference: Mol Cancer Ther. 2018 Oct;17(10):2091-2099. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/30045927/