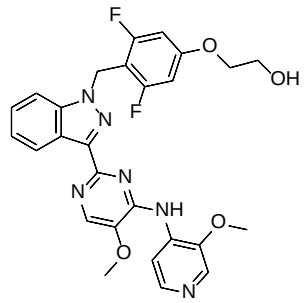
Product data sheet

MedKoo Cat#: 408069 Name: BAY-1816032 CAS#: 1891087-61-8 Chemical Formula: $C_{27}H_{24}F_2N_6O_4$ Exact Mass: 534.1827 Molecular Weight: 534.52	
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:
BAY-1816032 is a potent and oral available BUB1 (budding uninhibited by benzimidazoles 1) kinase inhibitor with an IC50 of 7 nM. BAY 1816032 showed long target residence time and induced chromosome mis-segregation upon combination with low concentrations of paclitaxel. It was synergistic or additive in combination with paclitaxel or docetaxel, as well as with ATR or PARP inhibitors in cellular assays. Tumor xenograft studies demonstrated a strong and statistically significant reduction of tumor size and excellent tolerability upon combination of BAY 1816032 with paclitaxel or olaparib as compared with the respective monotherapies.

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	37.50	70.16

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.87 mL	9.35 mL	18.71 mL
5 mM	0.37 mL	1.87 mL	3.74 mL
10 mM	0.19 mL	0.94 mL	1.87 mL
50 mM	0.04 mL	0.19 mL	0.37 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. Siemeister G, Mengel A, Fernández-Montalván AE, Bone W, Schröder J, Zitzmann-Kolbe S, Briem H, Prechtl S, Holton SJ, Mönning U, von Ahsen O, Johanssen S, Cleve A, Pütter V, Hitchcock M, von Nussbaum F, Brands M, Ziegelbauer K, Mumberg D. Inhibition of BUB1 Kinase by BAY 1816032 Sensitizes Tumor Cells toward Taxanes, ATR, and PARP Inhibitors In Vitro and In Vivo. Clin Cancer Res. 2019 Feb 15;25(4):1404-1414. doi: 10.1158/1078-0432.CCR-18-0628. Epub 2018 Nov 14. PMID: 30429199.

In vivo study

1. Siemeister G, Mengel A, Fernández-Montalván AE, Bone W, Schröder J, Zitzmann-Kolbe S, Briem H, Prechtl S, Holton SJ, Mönning U, von Ahsen O, Johanssen S, Cleve A, Pütter V, Hitchcock M, von Nussbaum F, Brands M, Ziegelbauer K, Mumberg D. Inhibition of BUB1 Kinase by BAY 1816032 Sensitizes Tumor Cells toward Taxanes, ATR, and PARP Inhibitors In Vitro and In Vivo. Clin Cancer Res. 2019 Feb 15;25(4):1404-1414. doi: 10.1158/1078-0432.CCR-18-0628. Epub 2018 Nov 14. PMID: 30429199.

7. Bioactivity
Biological target: BAY-1816032 is a BUB1 (budding uninhibited by benzimidazoles 1) kinase inhibitor with an IC50 of 7 nM.

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In vitro activity

BAY 1816032 abrogated histone H2A-Thr120 phosphorylation, the best validated substrate of BUB1 kinase, in nocodazole-arrested HeLa cells after 1 hour of compound incubation with an IC50 of 29 ± 23 nmol/L demonstrating its potent intracellular inhibition of BUB1 kinase activity. However, the functionality of the spindle assembly checkpoint was not affected by BUB1 kinase inhibition as indicated by persistent histone H3-Ser10 phosphorylation in nocodazole-arrested HeLa cells upon 4-hour incubation at concentrations up to 10 μmol/L.

Reference: Clin Cancer Res. 2019 Feb 15;25(4):1404-1414. https://clincancerres.aacrjournals.org/content/25/4/1404.long

In vivo activity

The combination of BAY 1816032 with paclitaxel was evaluated in the SUM-149 model of triple-negative breast cancer. Treatment of tumor-bearing female nude mice with BAY 1816032 as single agent did not show any significant effect on the growth of SUM-149 tumors (Fig. 3A). Paclitaxel initially suppressed tumor growth; however, starting around day 28, tumors gained size and grew out although the dose of paclitaxel had been increased from 8 mg/kg to the MTD of 20 mg/kg from day 24 onward. In contrast, the tumors from the BAY 1816032 plus paclitaxel combination treatment group grew much slower and entered a phase of stable disease around day 46. An analysis of the median tumor areas of the paclitaxel single-agent group and the combination group at day 54 showed a statistically significant difference between the two treatment groups ($P < 0.05$, ANOVA on ranks).

Reference: Clin Cancer Res. 2019 Feb 15;25(4):1404-1414. https://clincancerres.aacrjournals.org/content/25/4/1404.long