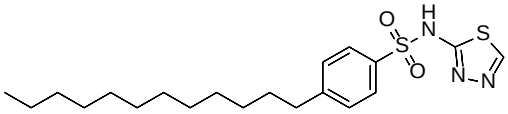
Product data sheet

MedKoo Cat#: 401705 Name: PHT-427 CAS: 1191951-57-1 Chemical Formula: $C_{20}H_{31}N_3O_2S_2$ Exact Mass: 409.1858 Molecular Weight: 409.607	
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:
PHT-427 is an AKT inhibitor that inhibits AKT and PDPK1 at low micromolar concentrations in numerous cancer cell lines and exhibits good oral anti-tumor activity in mouse xenograft models. PHT-427 reduces the phosphorylation of AKT and PDPK1. Following the administration of a single oral dose of PHT-427 to mice bearing BxPC-3 human pancreatic tumor xenografts, PHT-427 inhibited the phosphorylation of both Akt and PDPK1 as well as downstream targets maximally at 8–12 h after administration corresponding to its peak plasma concentration, with PDPK1 inhibition extending to 24 hr.

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
DMF	33.0	80.57
DMF:PBS (pH 7.2) (1:4)	0.2	0.49
DMSO	47.24	115.33

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.44 mL	12.21 mL	24.41 mL
5 mM	0.49 mL	2.44 mL	4.88 mL
10 mM	0.24 mL	1.22 mL	2.44 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. Li X, Wang Q, Zheng J, Guan Y, Liu C, Han J, Liu S, Liu T, Xiao C, Wang X, Liu Y. PHT427 as an effective New Delhi metallo-β-lactamase-1 (NDM-1) inhibitor restored the susceptibility of meropenem against Enterobacteriaceae producing NDM-1. Front Microbiol. 2023 Apr 17;14:1168052. doi: 10.3389/fmicb.2023.1168052. PMID: 37138606; PMCID: PMC10150926.

2. Yanes-Díaz J, Palao-Suay R, Aguilar MR, Riestra-Ayora JI, Ferruelo-Alonso A, Rojo Del Olmo L, Vázquez-Lasa B, Sanz-Fernández R, Sánchez-Rodríguez C. Antitumor Activity of Nanoparticles Loaded with PHT-427, a Novel AKT/PDK1 Inhibitor, for the Treatment of Head and Neck Squamous Cell Carcinoma. Pharmaceutics. 2021 Aug 12;13(8):1242. doi: 10.3390/pharmaceutics13081242. PMID: 34452203; PMCID: PMC8401941.

In vivo study

Product data sheet

1. Meuillet EJ, Zuohe S, Lemos R, Ihle N, Kingston J, Watkins R, Moses SA, Zhang S, Du-Cuny L, Herbst R, Jacoby JJ, Zhou LL, Ahad AM, Mash EA, Kirkpatrick DL, Powis G. Molecular pharmacology and antitumor activity of PHT-427, a novel Akt/phosphatidylinositide-dependent protein kinase 1 pleckstrin homology domain inhibitor. Mol Cancer Ther. 2010 Mar;9(3):706-17. doi: 10.1158/1535-7163.MCT-09-0985. Epub 2010 Mar 2. PMID: 20197390; PMCID: PMC2837366.

7. Bioactivity

Biological target:

PHT-427 is an inhibitor of the pleckstrin homology (PH) domain of Akt, and it is also an inhibitor of PDPK1 with Kis of 2.7 μM and 5.2 μM and for Akt and PDPK1.

In vitro activity

PHT427 was identified as an inhibitor of NDM-1. It could significantly inhibit the activity of NDM-1 with an IC50 of 1.42 μmol/L, and restored the susceptibility of meropenem against E. coli BL21(DE3)/pET30a(+)-bla NDM-1 and K. pneumoniae clinical strain C1928 (producing NDM-1) in vitro. The mechanism study indicated that PHT427 could act on the zinc ions at the active site of NDM-1 and the catalytic key amino acid residues simultaneously.

Reference: Front Microbiol. 2023 Apr 17;14:1168052. https://pubmed.ncbi.nlm.nih.gov/37138606/

In vivo activity

PHT-427 itself (C-12 chain) bound with the highest affinity to the PH domains of both PDPK1 and Akt. PHT-427 inhibited Akt and PDPK1 signaling and their downstream targets in sensitive but not resistant cells and tumor xenografts. When given orally, PHT-427 inhibited the growth of human tumor xenografts in immunodeficient mice, with up to 80% inhibition in the most sensitive tumors, and showed greater activity than analogues with C4, C6, or C8 alkyl chains. Inhibition of PDPK1 was more closely correlated to antitumor activity than Akt inhibition.

Reference: Mol Cancer Ther. 2010 Mar;9(3):706-17. https://pubmed.ncbi.nlm.nih.gov/20197390/

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.