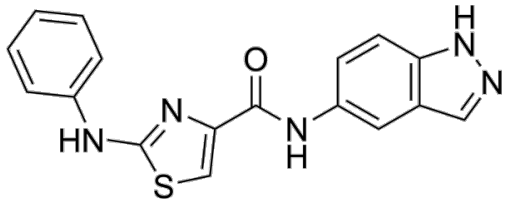
Product Data Sheet

Product Name: GPS167
Cat. No.: GC78961

Chemical Properties

Cas. No.	3034312-19-8		
Formula	$C_{17}H_{13}N_5OS$	M.Wt	335.38
Solubility		Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure			



Background

GPS167 is a CLK kinase inhibitor that potently and selectively inhibits recombinant human CLK1, CLK2 and CLK4. By inhibiting CLK-mediated phosphorylation of SRSF10, GPS167 upregulates the protein-binding ability of CLK1 and CLK4 with SRSF10, downregulates oncogenic BCLAF1-L and upregulates tumor-suppressive BCLAF1-S, regulates alternative splicing of genes such as MDM2 and MDM4, stabilizes p53 protein and induces DNA damage, ultimately triggering tumor cell apoptosis. GPS167 can block the epithelial-mesenchymal transition process of tumors, activate intracellular double-stranded RNA-mediated antiviral immune responses, and produce synergistic cytotoxicity when combined with microtubule-targeting drugs. GPS167 can be used in research

related to various cancers including colorectal cancer [1] [2] [3].

In Vitro, GPS167 potently and selectively inhibits recombinant human CLK1, CLK2 and CLK4 with IC_{50} values of 0.0896 μM, 0.0820 μM and 0.1230 μM, and shows weak or negligible activity against most other tested human kinases. In non-radioactive proximity assays, GPS167 yields an IC_{50} of 0.5069 μM for CLK1 and displays poor inhibitory potency toward DYRK1A and DYRK1B; and its inhibitory effect on SRSF10 phosphorylation is preferential than its inhibitory effect on SRSF1 phosphorylation[1][2]. GPS167 (1-30 μM; 6 h) increases Thr212-Tau phosphorylation in SH-SY5Y cells expressing human 4R-Tau[1]. GPS167 (48 h) is non-cytotoxic to HT22 murine hippocampal neuronal cells, with an IC_{50} for viability >100 μM[1]. GPS167 (0.05-100 μM; 48 h) modulates BCLAF1 alternative splicing in HCT116 cells, reducing BCLAF1-L variant levels with an EC50 of ~2 μM[2]. GPS167 (10-20 μM; 24 h cell incubation, 10 min pull-down incubation) promotes dephosphorylation of specific serine residues on SRSF10 and increases the interaction between SRSF10 and CLK1 in HCT116 cells[2]. GPS167 (10 μM; 0-80 h) induces potent cytotoxicity in human colorectal cancer cell lines (HCT116, COLO205, SW620) but has minimal effects on Caco-2 cells and normal colonocyte cell lines (CRL-1831, CRL-1790)[2]. GPS167 induces apoptosis in human colorectal cancer HCT116, COLO205 and SW620 cells accompanied by elevated cleaved PARP and cleaved caspase-3, whereas no apoptotic effect is observed in Caco-2 and normal colon epithelial CRL-1831 cells. It inhibits cancer cell migration as evidenced by decreased scratch wound closure rate[2]. GPS167 (10-20 μM; up to 120 h viability, up to 84 h cytotoxicity, 72 h PARP cleavage) impairs viability, induces cytotoxicity and apoptosis, and disrupts structure in human and mouse colorectal cancer organoids, but has minimal effects on normal colorectal organoids[2]. GPS167 (10-20 μM; 24 h viability and caspase activity, up to 72 h cytotoxicity) elicits p53-dependent growth inhibition, cytotoxicity, and apoptosis in HCT116 colorectal cancer cells, with increased p53 expression and DNA damage observed in p53-proficient cells[2]. GPS167 (8 days) in NALM-6 cells, depletion of genes involved in mitotic cell cycle checkpoint/chromosome segregation increases sensitivity to GPS167, while depletion of mitotic spindle assembly-related genes reduces GPS167 sensitivity[3]. GPS167 disrupts the expression and alternative splicing of EMT-relevant genes, including FLNB and CD44, in HCT116 colorectal cancer cells[3]. GPS167 (1 μM; 4 days) in MCF10A breast epithelial cells, upregulates the epithelial marker ECAD (both with and without TGF-β treatment) and inhibits TGF-β-induced EMT morphological changes, without altering mesenchymal

marker expression[3]. GPS167 (20 μM; up to 72 h) in HCT116 colorectal cancer cells, depletion of the dsRNA sensor DHX33 significantly reduces cytotoxicity over 72 hours[3]. GPS167 inhibits proliferation and induces p53-dependent apoptosis in multiple cancer cell lines (including colorectal, melanoma, leukemia, breast, ovarian, and renal) and colorectal organoids, while sparing normal colonocyte cells and organoids[3].

References:
[1]. Lindberg MF, et al. Comparative Efficacy and Selectivity of Pharmacological Inhibitors of DYRK and CLK Protein Kinases. J Med Chem. 2023;66(6):4106-4130.
[2]. Sohail M, et al. A novel class of inhibitors that target SRSF10 and promote p53-mediated cytotoxicity on human colorectal cancer cells. NAR Cancer. 2021;3(2):zcab019. Published 2021 May 25.
[3]. Shkreta L, et al. The anticancer potential of the CLK kinases inhibitors 1C8 and GPS167 revealed by their impact on the epithelial-mesenchymal transition and the antiviral immune response. Oncotarget. 2024 May 16;15:313-325.

Caution: Product has not been fully validated for medical applications. For research use only.
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