

Product Data Sheet

Product Name: GPS167
Cat. No.: GC78961

Chemical Properties

Cas. No. 3034312-19-8

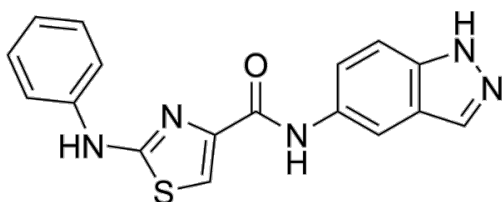
Formula $C_{17}H_{13}N_5OS$ M.Wt 335.38

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 sizes: 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

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

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

In Vitro, GPS167 potently and selectively inhibits recombinant human CLK1, CLK2 and CLK4 with IC₅₀ values of 0.0896 μ M, 0.0820 μ M and 0.1230 μ M, and shows weak or negligible activity against most other tested human kinases. In non-radioactive proximity assays, GPS167 yields an IC₅₀ of 0.5069 μ M 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 μ M; 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 IC₅₀ for viability >100 μ M^[1]. GPS167 (0.05-100 μ M; 48 h) modulates BCLAF1 alternative splicing in HCT116 cells, reducing BCLAF1-L variant levels with an EC₅₀ of ~2 μ M^[2]. GPS167 (10-20 μ M; 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 μ M; 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 μ M; 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 μ M; 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 μ M; 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

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marker expression^[3]. GPS167 (20 μ M; 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.

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