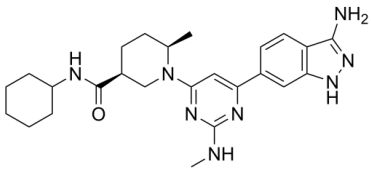
Data Sheet

Product Name:	GSK2334470
Cat. No.:	CS-0917
CAS No.:	1227911-45-6
Molecular Formula:	$C_{25}H_{34}N_8O$
Molecular Weight:	462.59
Target:	PDK-1
Pathway:	PI3K/Akt/mTOR
Solubility:	DMSO : ≥ 50 mg/mL (108.09 mM)



BIOLOGICAL ACTIVITY:

GSK2334470 is a highly specific and potent inhibitor of **PDK1** with an **IC_{50}** of 10 nM. IC50 & Target: IC50: 10 nM(PDK1)[1] ***In Vitro:*** Small molecule GSK2334470 inhibits PDK1 with an IC_{50} of ~10 nM, but does not suppress the activity of 93 other protein kinases including 13 AGC-kinases most related to PDK1 at 500-fold higher concentrations. Addition of GSK2334470 ablates T-loop residue phosphorylation and activation of SGK isoforms and S6K1 induced by serum or IGF-1 (insulin-like growth factor 1). GSK2334470 and AZD8055 effectively inhibite phosphorylation of PDK1 and mTOR, respectively, and induce higher G0–G1 ratio in LAN-1-MK than that in LAN-1 as well. PDK1 and mTOR inhibitors effecte on phosphorylation of GSK3β in some of resistant sublines[2]. ***In Vivo:*** The efficacy of the PDK1 inhibitor (PDKi) GSK2334470 is tested in newborn $Braf^{V600E}::Pten^{-/-}$mice subjected to systemic administration of 4-HT. Twice weekly administration of PDK1 results in marked inhibition of pigmented lesions and concomitant melanomagenesis, as well as significant inhibition of lung metastases, seen by H&E staining-based quantification (~80%), and lymph node metastases as by S100 immunostaining, similar to the phenotype seen upon genetic ablation of ***Pdk1***[3].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [2]GSK2334470 is dissolved in DMSO and diluted with appropriate medium before use. To study the inhibitory effect of GSK2334470 on mTOR-S6K pathway, non-resistant cells and the resistant sublines are treated with GSK2334470 at 5 μM for 1.5 and 12 h in 10 % FBS medium with/without MK-2206 (5 μM)[2]. **Animal Administration:** [3]Mice is dissolved in DMSO and then diluted with PBS or saline. $Braf^{V600E}::Pten^{-/-}$ are generated as previously described. Cohorts of six animals per group are used in each experimental group. GSK2334470 is administered through IP injection (100 mg/kg) 3 times per week starting the same day of topical administration of 4-hydroxytamoxifen and ending at the time of mouse collection, based on earlier studies[3].

References:

[1]. Najafov A, et al. Characterization of GSK2334470, a novel and highly specific inhibitor of PDK1. Biochem J.?2011 Jan 15;433(2):357-69.

[2]. Qi L, et al. PDK1-mTOR signaling pathway inhibitors reduce cell proliferation in MK2206 resistant neuroblastoma cells. Cancer Cell Int.?2015 Sep 29;15:91.

[3]. Scortegagna M, et al. Genetic inactivation or pharmacological inhibition of Pdk1 delays development and inhibits metastasis of Braf(V600E)::Pten(-/-) melanoma. Oncogene. 2014 Aug 21;33(34):4330-9.

CAIndexNames:

3-Piperidinecarboxamide, 1-[6-(3-amino-1H-indazol-6-yl)-2-(methylamino)-4-pyrimidinyl]-N-cyclohexyl-6-methyl-, (3S,6R)-

SMILES:

O=C([C@@H]1CN(C2=NC(NC)=NC(C3=CC4=C(C=C3)C(N)=NN4)=C2)[C@H](C)CC1)NC5CCCCC5

Tel: 610-426-3128 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA