GSK2334470

Cat. No.: HY-14981

CAS No.: 1227911-45-6

Molecular Formula: $C_{25}H_{34}N_8O$

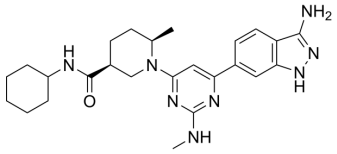
Molecular Weight: 462.59

Target: PDK-1

Pathway: PI3K/Akt/mTOR

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (108.09 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1617 mL	10.8087 mL	21.6174 mL
5 mM	0.4323 mL	2.1617 mL	4.3235 mL
10 mM	0.2162 mL	1.0809 mL	2.1617 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.40 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.40 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.40 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK2334470 is a highly specific and potent inhibitor of PDK1 with an IC_{50} of 10 nM.

IC_{50} & 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Br J Cancer. 2020 Aug;123(4):542-555.
- Neurobiol Dis. 2021 Jan;148:105212.
- J Biol Chem. 2023 Apr 12;104699.
- Programa de Doctorado en Biomedicina. 2020 Sep.

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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.

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

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