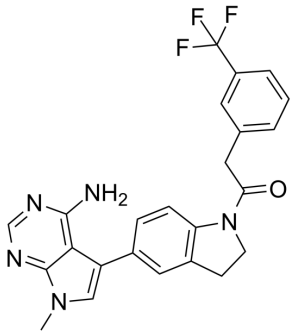
GSK2606414

Cat. No.:	HY-18072
CAS No.:	1337531-36-8
Molecular Formula:	$C_{24}H_{20}F_3N_5O$
Molecular Weight:	451.44
Target:	PERK; Autophagy; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Autophagy; Apoptosis
Storage:	4°C, protect from light * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (221.51 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2151 mL	11.0757 mL	22.1513 mL
5 mM	0.4430 mL	2.2151 mL	4.4303 mL
10 mM	0.2215 mL	1.1076 mL	2.2151 mL

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

In Vivo

1. Add each solvent one by one: 0.5% HPMC >> 0.2%Tween80
   Solubility: 3.33 mg/mL (7.38 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.54 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.54 mM); Suspended solution; Need ultrasonic
4. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (5.54 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK2606414 is a cell-permeable and orally available protein kinase R-like endoplasmic reticulum (ER) kinase (PERK) inhibitor with an IC_{50} of 0.4 nM.

IC_{50} & Target			
	EIF2AK3 (PERK) 0.4 nM (IC_{50})	EIF2AK1 (HRI) 420 nM (IC_{50})	EIF2AK2 (PKR) 696 nM (IC_{50})

In Vitro	GSK2606414 inhibits PERK activation in cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	GSK2606414 (50 and 150 mg/kg, p.o.) inhibits the growth of a human tumor xenograft in mice[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Exponentially growing BxPC3 tumor cells (10×10^6 cells/mouse) from cell culture are implanted subcutaneously into the right flank of female nude mice. Sixteen days after implantation, mice with -200 mm^3 tumors are randomized into various treatment groups (n=8 mice/group). Animals are orally treated with vehicle (0.5% hydoxypropylmethylcellulose, 0.1% Tween 80 in water, pH 4.8), compound at 50 or 150 mg/kg, b.i.d. for 21 days. Tumor volume is measured twice weekly with calipers and calculated. Results are represented as percent inhibition on completion of dosing, which is 100[1-(average growth of drug-treated population)/(average growth of vehicle-treated control population)]. Statistical analysis is performed using a two-tailed t test. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nature. 2023 Apr;616(7956):348-356.
- Nat Immunol. 2022 Jul;23(7):1021-1030.
- Cell Host Microbe. 2017 Dec 13;22(6):766-776.e4.
- Cell Metab. 2021 Mar 2;33(3):598-614.e7.
- Biomaterials. 2021, 120757.

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REFERENCES

[1]. Axten JM, et al. Discovery of 7-methyl-5-(1-{[3-(trifluoromethyl)phenyl]acetyl}-2,3-dihydro-1H-indol-5-yl)-7H-pyrrolo[2,3-d]pyrimidin-4-amine (GSK2606414), a potent and selective first-in-class inhibitor of protein kinase R (PKR)-like endoplasmic reticulu

[2]. Zhang M, et al. Inhibiting the Plasmodium eIF2α Kinase PK4 Prevents Artemisinin-Induced Latency. Cell Host Microbe. 2017 Dec 13;22(6):766-776.e4.

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