GSK1059615

Cat. No.: HY-12036

CAS No.: 958852-01-2

Molecular Formula: $C_{18}H_{11}N_3O_2S$

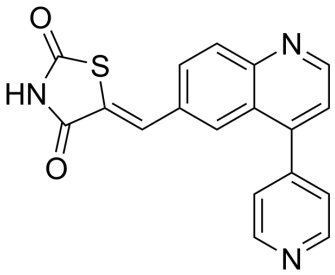
Molecular Weight: 333.36

Target: PI3K; mTOR; Apoptosis

Pathway: PI3K/Akt/mTOR; Apoptosis

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 : 5 mg/mL (15.00 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.9998 mL	14.9988 mL	29.9976 mL
	5 mM	0.6000 mL	2.9998 mL	5.9995 mL
	10 mM	0.3000 mL	1.4999 mL	2.9998 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: 0.5 mg/mL (1.50 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 0.5 mg/mL (1.50 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 0.5 mg/mL (1.50 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK1059615 is a dual inhibitor of PI3Kα/β/δ/γ (reversible) and mTOR with IC_{50} of 0.4 nM/0.6 nM/2 nM/5 nM and 12 nM, respectively.

IC_{50} & Target

PI3Kα	PI3Kβ	PI3Kγ	PI3Kδ
0.4 nM (IC_{50})	0.6 nM (IC_{50})	2 nM (IC_{50})	5 nM (IC_{50})

mTOR
12 nM (IC_{50})

In Vitro	GSK1059615 inhibits PI3Kα, β, γ and δ, with K_i of 0.42 nM, 0.6 nM, 0.47 nM and 1.7 nM, respectively[1]. In T47D and BT474 cancer cells, GSK1059615 inhibits the phosphorylation of Akt at S473, with IC_{50} of 40 nM[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	GSK1059615 (25 mg/kg) effectively inhibits tumor growth in xenograft mice models of BT474 or HCC1954 breast cancer cells [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [2]	The measurement of the GSK1059615-dependent inhibition of the PI3Ks is accessed using a HTRF based PI3K profiling assay kit. 400 pM enzyme is used in PI3Kα and δ assays, 200 pM in PI3Kβ assays, and 1 nM in PI3Kγ assay. In addition, the PI3Kα, β, and δ assays are run with 150 mM NaCl and 100 μM ATP, while the PI3Kγ assay is run with no NaCl and 15 μM ATP. All reactions are run at 10 μM PIP2. GSK1059615 is serially diluted (3-fold in DMSO), and 50 nL is transferred to a 384-well low-volume assay plate. PI3K Reaction Buffer is prepared by diluting the stock 1:4 with de-ionized water. Freshly prepared DTT is added at a final concentration of 5 mM on the day of use. Enzyme addition and GSK1059615 pre-incubation are initiated by the addition of 2.5 μL of PI3K in reaction buffer. Plates are incubated at room temperature for 15 min. Reactions are initiated by addition of 2.5 μL of 2× substrate solution (PIP2 and ATP in 1× reaction buffer). Plates are incubated at room temperature for one hour. Reactions are quenched by the addition of 2.5 μL of stop solution. The quenched reactions are then processed to detect product formation by adding 2.5 μL of Detection Solution. Following a 1-hour incubation in the dark, the HTRF signal is measured on the Envision plate reader set for 330 nm excitation and dual emission detection at 620 nm (Eu) and 665 nm (APC). The IC_{50} value is then obtained. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	Cells are plate at a density of 1×10^4 cells per well in clear flat-bottomed 96-well plates and incubated overnight. Then, GSK1059615 is added and the plates are incubated for 30 min. At the end of incubation, media is aspirated from the plates, and the plate is wash once with cold PBS. 80 μL MSD Lysis buffer is added into each well and the plates are incubated on a shaker at 4°C for at least 30 min. For Akt duplex assay, plates are washed with 200 μL/well wash buffer for 4 times and tapped on paper towel to blot. Then, 60 μL lysates is added to each well and the plates are incubated on shaker at room temperature for 1 hour. After another 4 times washing, antibody is added (25 μL per well) and the plates are incubated on shaker for 1 hour and washed again. Finally, Read Buffer is added (150 μL per well) and the plates are read immediately. IC_{50} values are then obtained. 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.
- Nat Commun. 2021 Nov 16;12(1):6607.
- Front Pharmacol. 2020 Nov 11;11:580407.
- Molecules. 2020 Apr 23;25(8):1980.
- bioRxiv. 2023 Feb 8.

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REFERENCES

[1]. Carnero A. Novel inhibitors of the PI3K family. Expert Opin Investig Drugs. 2009 Sep;18(9):1265-77.

[2]. Maira SM, et al. From the bench to the bed side: PI3K pathway inhibitors in clinical development. Curr Top Microbiol Immunol, 2010, 347, 209-239.

[3]. Takashi Kei Kishimoto, et al. Methods and compositions for attenuating gene therapy anti-viral transfer vector immune responses. US 20160074531 A1.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

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