# 产品名称：GSK1059615
# 产品别名：GSK1059615

## 生物活性：

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| **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 | PI3Kδ | PI3Kγ | mTOR |
|---|---|---|---|---|---|
| | 0.4 nM ($IC_{50}$) | 0.6 nM ($IC_{50}$) | 5 nM ($IC_{50}$) | 2 nM ($IC_{50}$) | 12 nM ($IC_{50}$) |

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| **In Vitro** | GSK1059615 inhibits PI3Kα, β, γ and δ, with Ki 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 IC50 of 40 nM[2]. |
| **In Vivo** | GSK1059615 (25 mg/kg) effectively inhibits tumor growth in xenograft mice models of BT474 or HCC1954 breast cancer cells[1]. |

**Solvent&Solubility**

***In Vitro:***

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

**$H_2O$ : < 0.1 mg/mL** (insoluble)

| **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 |

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

***In Vivo:***

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: 0.5 mg/mL (1.50 mM); Suspended solution; Need ultrasonic

此方案可获得 0.5 mg/mL (1.50 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

以 1 mL 工作液为例，取 100 μL 5.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)

Solubility: 0.5 mg/mL (1.50 mM); Suspended solution; Need ultrasonic

此方案可获得 0.5 mg/mL (1.50 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

以 1 mL 工作液为例，取 100 μL 5.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。

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| | 3.请依序添加每种溶剂： 10% DMSO →90% corn oil<br>Solubility: ≥ 0.5 mg/mL (1.50 mM); Clear solution<br>此方案可获得 ≥ 0.5 mg/mL (1.50 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。<br>以 1 mL 工作液为例，取 100 μL 5.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。 |
| **References** | [1]. Carnero A. Novel inhibitors of the PI3K family. Expert Opin Investig Drugs. 2009 Sep;18(9):1265-77.<br>[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.<br>[3]. Takashi Kei Kishimoto, et al. Methods and compositions for attenuating gene therapy anti-viral transfer vector immune responses. US 20160074531 A1. |

**实验参考：**

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| **Cell Assay** | Cells are plate at a density of $1\times10^4$ 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. [2] |
| **Kinase Assay** | 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. [2] |
| **References** | [1]. Carnero A. Novel inhibitors of the PI3K family. Expert Opin Investig Drugs. 2009 Sep;18(9):1265-77.<br>[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.<br>[3]. Takashi Kei Kishimoto, et al. Methods and compositions for attenuating gene therapy anti-viral transfer vector immune responses. US 20160074531 A1. |