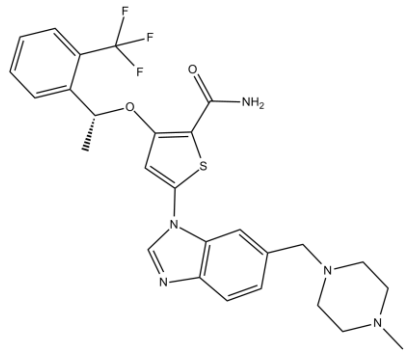
Product Name: GSK461364

Revision Date: 6/30/2018

Product Data Sheet

Chemical Properties



Product Name: GSK461364

Cas No.: 929095-18-1

M.Wt: 543.6

Formula: C27H28F3N5O2S

Synonyms: N/A

Chemical Name: 5-[6-[(4-methylpiperazin-1-yl)methyl]benzimidazol-1-yl]-3-[(1R)-1-[2-(trifluoromethyl)phenyl]ethoxy]thiophene-2-carboxamide

Canonical SMILES: CC(C1=CC=CC=C1C(F)(F)F)OC2=C(SC(=C2)N3C=NC4=C3C=C(C=C4)CN5CCN(CC5)C)C(=O)N

Solubility: ≥15.65mg/mL in Ethanol

Storage: Store at -20°C

General tips: For obtaining a higher solubility , please warm the tube at 37° C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20° C for several months.

Shopping Condition: Evaluation sample solution : ship with blue ice
All other available size: ship with RT , or blue ice upon request

Biological Activity

Targets : Cell Cycle/Checkpoint

Pathways: PLK

Description:

GSK461364 is a potent and reversible ATP competitive Plk1 inhibitor. Polo-like kinases (Plk) are a family of serine threonine kinases that are critical regulators of DNA damage response and cell cycle progression.
In vitro: GSK461364 showed at least 390-fold greater selectivity for Plk1 than for Plk2 and Plk3 and 1,000-fold greater than for 48 other kinases. The drug showed antiproliferative activity

against multiple (>120) tumor cell lines and potently inhibited the proliferation of greater than 83% and 91% of these cell lines [1].
In vivo: Intraperitoneal administration of GSK461364 caused regression or tumor growth delay in different xenograft models. In vivo suppression of Plk1 by using GSK461364 resulted in mitotic arrest with aberrant mitotic figures consisting of monopolar or collapsed mitotic spindles [1].
Clinical trial: The final recommended phase II dose for GSK461364 was 225 mg administered intravenously. Moreover, GSK461364 was suggested to involve coadministration of prophylactic anticoagulation for further clinical evaluation [1].

***Reference**:*
[1] Olmos D, Barker D, Sharma R, Brunetto AT, Yap TA, Taegtmeyer AB, Barriuso J, Medani H, Degenhardt YY, Allred AJ, Smith DA, Murray SC, Lampkin TA, Dar MM, Wilson R, de Bono JS, Blagden SP. Phase I study of GSK461364, a specific and competitive Polo-like kinase 1 inhibitor, in patients with advanced solid malignancies. Clin Cancer Res. 2011 May 15;17(10):3420-30.

Protocol

Cell experiment:

Cell lines	Human adult glioblastoma T98G cell lines and pediatric SF188 cell lines
Preparation method	The solubility of this compound in DMSO is > 15.65 mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37 ℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.
Reacting conditions	
Applications	After 72 h treatment, GSK461364 caused a significant decrease of proliferation in GBM T98G cells and SF188 cells.

Animal experiment [3]:

Animal models	18 years or older patients with a confirmed diagnosis of advanced solid tumor for which no effective treatment was available.
Dosage form	Intravenous infusion, 50 mg, once a week or 25 mg, twice a week, dose was escalated with treatment
Applications	After the end of the 4-hour infusion, GSK461364 plasma concentrations declined bi-exponentially. Distribution of GSK461364 was initially rapid and plasma concentrations decreased to approximately 15% to 20% of the Cmax within 8 hours of cessation of infusion.

Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

Reference:
[1]. Pezuk J A, Brassesco M S, Morales A G, et al. Polo-like kinase 1 inhibition causes decreased proliferation by cell cycle arrest, leading to cell death in glioblastoma[J]. Cancer gene therapy, 2013, 20(9): 499-506.
[2]. Olmos D, Barker D, Sharma R, et al. Phase I study of GSK461364, a specific and competitive Polo-like kinase 1 inhibitor, in patients with advanced solid malignancies[J]. Clinical Cancer Research, 2011, 17(10): 3420-3430.

Product Citations

1. Velpurisiva P, Piel BP, et al. "GSK461364A, a Polo-Like Kinase-1 Inhibitor Encapsulated in Polymeric Nanoparticles for the Treatment of Glioblastoma Multiforme (GBM)." Bioengineering (Basel). 2018 Oct 9;5(4). pii: E83. PMID:30304810
2. Higuchi F, Fink AL, et al. "PLK1 inhibition targets Myc-activated malignant glioma cells irrespective of mismatch repair deficiency-mediated acquired resistance to temozolomide." Mol Cancer Ther. 2018 Sep 14. pii: molcanther.0177.2018. PMID:30217967

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

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