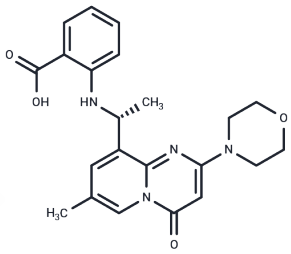
Data Sheet (Cat.No.T6087)

TargetMol

AZD 6482

Chemical Properties



CAS No. : 1173900-33-8

Formula: C22H24N4O4

Molecular Weight: 408.45

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	AZD 6482 (KIN-193) is a potent and selective inhibitor of p110β and PI3Kβ with IC50 values of 0.69nM and 10nM, respectively. AZD 6482 is particularly effective in blocking AKT signaling and tumor growth dependent on p110β activation or PTEN loss.
Targets(IC50)	Autophagy,DNA-PK,PI3K
In vitro	**METHODS**: U87 and U118 cells were treated with AZD 6482 (KIN-193) (0.625, 1.25, 2.5, 5, 10, 20, 40 μM, 48 hours), and CCK8 was used to measure its inhibitory effect on the proliferation of U87 and U118 cells. **RESULTS** AZD 6482 inhibited the viability of both cell lines in a dose-dependent manner, with U118 cells being more sensitive than U87 cells, with IC50 values of 7.989 and 9.061 μM, respectively. [4]
In vivo	**METHODS**: Mice with HCC70, PC3, and HCC1954 xenograft tumors were treated with AZD 6482 (KIN-193) (20 mg/kg, i.p., twice daily) or GDC-0941 (150 mg/kg, orally, once daily). Study the in vivo effects of KIN-193 on PTEN-deficient tumors. **RESULTS** AZD 6482 significantly inhibited tumor growth of HCC70 and PC3 tumors but failed to block the growth of HCC1954 tumors. [2]
Kinase Assay	Assay of PI3K enzyme inhibition: The inhibition of PI3Kβ, PI3Kα, PI3Kγ, and PI3Kδ is evaluated in an AlphaScreen based enzyme activity assay using human recombinant enzymes. The assay measures PI3K-mediated conversion of PIP2 to PIP3. Biotinylated PIP3, a GST-tagged pleckstrin homology (PH) domain and the two AlphaScreen beads form a complex that elicits a signal upon laser excitation at 680 nm. The PIP3 formed in the enzyme reaction competes with the biotinylated PIP3 for binding to the PH domain thus reducing the signal with increasing enzyme product. The AZD6482 is dissolved in DMSO and added to 384 well plates. PBKβ, PBKα, PBKγ, or PBKδ is added in a Tris buffer (50 mM Tris pH 7.6, 0.05% CHAPS, 5 mM DTT, and 24 mM MgCl2) and allowed to preincubate with AZD6482 for 20 minutes prior to the addition of substrate solution containing PIP2 and ATP. The enzyme reaction is stopped after 20 minutes by addition of stop solution containing EDTA and biotin-PIP3, followed by addition of detection solution containing GST-grpl PH and AlphaScreen beads. Plates are left for a minimum of 5 hours in the dark prior to analysis. The final concentration of DMSO, ATP and PIP2 in the assay are, 0.8%, 4 μM, and 40 μM, respectively. IC50 values are calculated according to the equation, y = {a+[(b-a)/(l+(x/IC50)s)]}, where y = % inhibition; a = 0%; b = 100%; s = the slope of the concentration-response curve; x = AZD6482 concentration.

Cell Research	For assay of washed platelet aggregation (WPA), the platelet pellets are isolated from human blood and re-suspended to 2 × 1015/L in Tyrodes buffer (TB) containing 1 μM hirudin and 0.02 U/mL apyrase. Then, the platelet suspension is left to rest at room temperature for 30 min. Just prior to time for assay, CaCl2 is added to a final concentration of 2 mM. AZD6482, dissolved in DMSO, is added to a 96-well plate prior to the addition of the washed platelet suspension. The platelet suspension is preincubated with AZD6482 for 5 min. Light absorption at 650 nm is recorded before and after a 5 min plate shake and referred to as recording 0 (R0) and Rl. A mouse anti-human CD9 antibody is added (at a donor specific concentration) to each well prior to next 10 min plate shake and light absorption recording; R2. For data analysis, light absorbance in wells with TB are subtracted from all readings before percent aggregation is calculated according the formula: [(R1-R2)/R1] × 100 = % aggregation. Spontaneous aggregation or pro-aggregatory effect of the inhibitor is evaluated by the same formula, [(R0-Rl)/R0] × 100 = % aggregation. IC50 values are calculated according to the equation, y = {a+[(b-a)/(l+(x/IC50)s)]}, where y = % inhibition; a = 0%; b = 100%; s = the slope of the concentration-response curve; x = AZD6482 concentration. (Only for Reference)

Solubility Information

Solubility	DMSO: 45 mg/mL (110.17 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (4.9 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.4483 mL	12.2414 mL	24.4828 mL
5 mM	0.4897 mL	2.4483 mL	4.8966 mL
10 mM	0.2448 mL	1.2241 mL	2.4483 mL
50 mM	0.049 mL	0.2448 mL	0.4897 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Thaiparambil J,et al. Integrative metabolomics and transcriptomics analysis reveals novel therapeutic vulnerabilities in lung cancer. Cancer Med. 2023 Jan;12(1):584-596.
Ni J, et al. Functional characterization of an isoform-selective inhibitor of PI3K-p110β as a potential anticancer agent. Cancer Discov. 2012 May;2(5):425-33.
Nylander S, et al. Human target validation of phosphoinositide 3-kinase (PI3K)β: effects on platelets and insulin sensitivity, using AZD6482 a novel PI3Kβ inhibitor. J Thromb Haemost. 2012 Oct;10(10):2127-36.
Xu PF, et al. PI3Kβ inhibitor AZD6482 exerts antiproliferative activity and induces apoptosis in human glioblastoma cells. Oncol Rep. 2019 Jan;41(1):125-132.