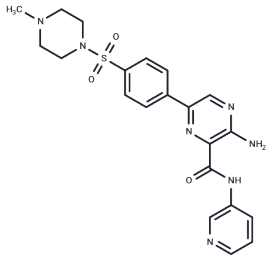
Data Sheet (Cat.No.T1957)

TargetMol

AZD2858

Chemical Properties



CAS No. : 486424-20-8

Formula: C21H23N7O3S

Molecular Weight: 453.52

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	AZD2858 is a selective GSK-3 inhibitor, inhibiting tau phosphorylation at the S396 site and activating Wnt signaling pathway.
Targets(IC50)	GSK-3
In vitro	After three weeks of treatment with 30 μM/kg AZD2858, rats exhibited increases in bone callus mineral density (28% at 2 weeks, 38% at 3 weeks) and mineral content (81% at two weeks, 93% at three weeks). Treatment with AZD2858 for 28 days resulted in time-dependent changes in serum markers of bone turnover, along with an increase in bone density. Within 7 days of AZD2858 treatment, the bone formation marker P1NP increased, and the resorption marker TRAcP-5b decreased, indicating enhanced bone metabolism and reduced absorption in rats. Oral administration of AZD2858 for two weeks led to a dose-dependent increase in bone density compared to the control group, with the greatest efficacy observed at a daily dose of 20 mg/kg (total BMC: 172% of the control group). AZD2858 treatment expedited bone fracture healing, with the presence of a bony callus and no significant cartilage components.
In vivo	AZD2858 induces β-catenin stabilization in human and rat mesenchymal stem cells, activating osteoblasts and osteogenic mineralization in vitro. Treatment with AZD2858 (1 μM, 12 hours) on primary isolated human osteoblast-like cells results in a three-fold increase in β-catenin levels.
Kinase Assay	Tau phosphorylation assay: NIH-3T3 cells expressing 4-repeat Tau are used to assess functional activity of AZD2858 in vitro. The cells are grown in DMEM media and 2 mM L-glut, and 10% HiFCS, and plated at a concentration of 6×105 cells/well in 6-well plates. In each experiment, AZD2858 is dosed in triplicates at a concentration of 1, 10, 100, 500, 1000, 2000 and 10,000 nM. Cells are treated for 4 h prior to cell lysis using 100 μL ice cold lysis buffer (0.5% NP-40, 10 mM Tris, pH 7.2, 150 mM NaCl, 2 mM EDTA). A suspension is made with addition of protease and phosphatase inhibitors: 50 mM NaF, 0.2 mM NaVO4 and Cocktail Protease inhibitors. The solution is then snap frozen at ? 80 ° C for at least 1 h, before thawing on ice and lysate clarification by centrifugation, followed by Western blot according to standard protocols. After blocking, the blots are exposed to the primary antibody, Phospho-Ser396-tau (1:1000) over night, washed and incubated with the secondary antibody (donkey anti-rabbit, 1:5000), followed by a final wash. For re-probing, the primary antibody Tau5 (1:200) and the secondary horseradish peroxidase linked antibody (sheep anti-mouse, 1:10000) are used. All blots are developed using ECL Western blot detection reagents, Kodak X-ray films, quantified

	using densitometric analysis, and the ratio of S396 tau to total tau (tau5) is calculated.
Cell Research	Human adipose derived stem cells and rat MSCs (isolated from bone marrow of Sprague Dawley rats at less than 8 weeks after gestation) are cultured in a basal media of DMEM containing 5% FBS and 2 mM GlutaMax. Cells are seeded in basal media into 96-well plates (3-5000 cells/well) for 18 h before treatment with AZD2858 (0.3 nM to 20 mM). After 24 h, β-catenin stabilisation is measured.(Only for Reference)

Solubility Information

Solubility	Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 7 mg/mL (15.43 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.205 mL	11.0249 mL	22.0497 mL
5 mM	0.441 mL	2.205 mL	4.4099 mL
10 mM	0.2205 mL	1.1025 mL	2.205 mL
50 mM	0.0441 mL	0.2205 mL	0.441 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.

Reference

Marsell R, et al. Bone, 2012, 50(3), 619-627.
Gilmour PS, Toxicol Appl Pharmacol, 2013, 272(2), 399-407.
Sisask G, et al. Bone, 2013, 54(1), 126-132.