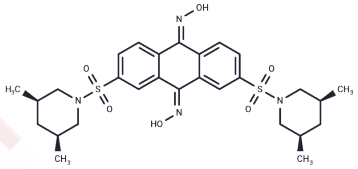
Data Sheet (Cat.No.T5642)

TargetMol

Tegatrabetan

Chemical Properties



CAS No. : 1227637-23-1

Formula: C28H36N4O6S2

Molecular Weight: 588.74

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	Tegatrabetan (BC2059) is a small molecule inhibitor of the Wnt/beta-catenin pathway with potential antineoplastic activity.
Targets(IC50)	Wnt/beta-catenin
In vitro	BC2059 induces apoptosis in primary multiple myeloma samples in vitro, causing minimal apoptosis on healthy peripheral blood mononuclear cells[1].
In vivo	BC2059 synergizes with the proteasome inhibitor bortezomib both in HMCL and primary multiple myeloma samples. Finally, in xenograft models of human myelomatosis, BC2059 delays tumor growth and prolongs survival with minor on-target side effects. Collectively, these results demonstrate the efficacy of targeting the Wnt/β-catenin pathway with BC2059 both in vitro and in vivo, at clinically achievable doses[1].
Cell Research	For β-catenin knockdown, 2 mL of 2 × 10^5/mL KMS18 cells were plated into a 12-well plate at day 0 (KMS18 doubling time: 36 hours).?At day 1, media were replaced by 1 mL of Opti-MEM , and transfection was carried out with Lipofectamine RNAiMAX .?For β-catenin knockdown, we used SignalSilence β-catenin siRNA I and β-catenin siRNA II (Cell Signaling Technology) at concentrations recommended by the manufacturer, whereas Silencer Negative Control No. 1 siRNA ?was used as a negative control, at the same concentration.?Six hours after the transfection, 1 mL of fresh media (RPMI-10% FCS) was added in every well.?At days 2 and 3, cells were treated with BC2059 (50, 100, 150 nmol/L) and then harvested at day 4 (72 hours after transfection).?Cell death was monitored by PI staining with FACS, whereas untreated cells were collected for β-catenin protein level measurement by immunoblotting.?Cells were lysed with RIPA lysis buffer, and 70 μg of protein was separated by 6% SDS-PAGE and blotted onto PVDF as already described.?β-Actin (mouse mAb HRP conjugate;?Cell Signaling Technology) was used as a loading control[1].
Animal Research	Adult age-matched Cg-Prkdcscid Il2rgtm1Wjl/SzJ mice were injected (intravenously) with 1 × 10^6 U266 HMCL, carrying the FUL2-TGvector .?At day 21, a limited course of treatment was commenced after confirmation of established measurable disease by bioluminescence.?Control mice (n = 4) received 17% Solutol HS 15 whereas treated mice received 5 (n = 4) or 10 mg/kg BC2059 (n = 5) twice a week intravenously for 3 consecutive weeks (6 doses in total).?Tumor burden was monitored on a weekly basis by in vivo imaging, from the second week of the experiment (day 18) until the first mice reached scientific endpoints.?Briefly, mice were anaesthetized, injected intraperitoneally

Animal Research	with 125 mg/kg luciferin, and imaged with the Lumina III XR system.?Acquisition and analysis were performed with the Living Image system.?Peripheral blood counts were evaluated sequentially during the course of the experiment .Upon reaching scientific endpoints (hind limp paralysis, >20% weight loss), mice were humanely euthanized and tissues (skin and colon) were collected.?Tissues were formalin fixed and embedded in paraffin, sectioned, and stained with H&E and β-catenin antibody.?Images were taken with an Olympus BX51 microscope[1].

Solubility Information

Solubility	DMSO: 250 mg/mL (424.64 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+90% Corn Oil: 2.5 mg/mL (4.25 mM),Sonication is recommended. 10% DMSO+40% PEG300+5% Tween 80+45% Saline: 10 mg/mL (16.99 mM),Suspension. 10% DMSO+90% Saline: < 10 mg/mL (16.99 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. *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	1.6985 mL	8.4927 mL	16.9854 mL
5 mM	0.3397 mL	1.6985 mL	3.3971 mL
10 mM	0.1699 mL	0.8493 mL	1.6985 mL
50 mM	0.034 mL	0.1699 mL	0.3397 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

Savvidou I, Khong T, Cuddihy A, et al. Beta-catenin inhibitor BC2059 is efficacious as monotherapy or in combination with proteasome inhibitor bortezomib in multiple myeloma[J]. Molecular Cancer Therapeutics, 2017, 16(9):molcanther.0624.2016.

Ueda K, Kumari R, Schwenger E, et al. MDMX acts as a pervasive preleukemic-to-acute myeloid leukemia transition mechanism. Cancer cell. 2021, 39(4): 529-547. e7.

Fiskus W, Sharma S, Saha S, et al. Pre-clinical efficacy of combined therapy with novel β-catenin antagonist BC2059 and histone deacetylase inhibitor against AML cells[J].Leukemia. 2015 Jun;29(6):1267-78