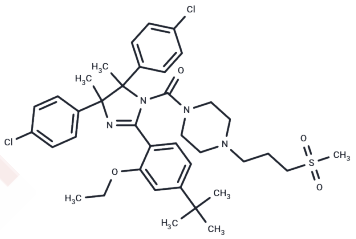
Data Sheet (Cat.No.T6965)

TargetMol

RG7112

Chemical Properties



CAS No. : 939981-39-2

Formula: C38H48Cl2N4O4S

Molecular Weight: 727.78

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	RG7112 (RO5045337) (RO5045337) is an orally bioavailable and selective p53-MDM2 inhibitor.
Targets(IC50)	Mdm2,E1/E2/E3 Enzyme,MDM-2/p53
In vitro	In three wild-type p53 (HCT116, RKO, and SJSA1) cell lines, RG7112 selectively and dose-dependently inhibits cell growth. In cancer cells expressing wild-type p53, RG7112 activates the p53 pathway, and induces cell-cycle arrest and apoptosis. RG7112, both alone and combined with Peg-IFNα 2a, significantly decreases MPN colony-forming unit-granulocyte macrophage and burst-forming unit-erythroid numbers and preferentially eliminates the total number of JAKV617F(+) MPN hematopoietic progenitor cells. In addition, in MDM2-amplified liposarcoma cells, RG7112 significantly synergizes with Trabectedin.
In vivo	In rats, RG7112 impairs thrombopoiesis via activation of p53. In the SJSA1 xenograft mouse model, RG7112 (200 mg/kg, p.o.) penetrates tumor cells and activate p53 and its 2 major functions, cell-cycle arrest and apoptosis. In nude mice bearing SJSA-1, and MHMn xenografts, RG7112 (100 mg/kg, p.o.) causes tumor regression.
Kinase Assay	HTRF assay: Homogeneous time-resolved fluorescence (HTRF) assay measures the signal generated by 2 components when they are in close proximity. The p53-MDM2 binding assay uses a biotinylated peptide derived from the MDM2-binding domain of p53 and a truncated N-terminal portion of recombinant human GST-tagged MDM2 protein containing the p53-binding domain. Proteins for crystal structure studies are expressed in E. coli strain BL21 using the helper plasmid pUBS 520 coding for the lacIq repressor and the rare tRNAArg [AGA/AGG]. For crystallization, the frozen protein is thawed and concentrated to 9.8 mg/mL using a Centricon concentrator (3,000 MW cutoff). The complex is then formed by combining the protein with a slight molar excess of the inhibitor (stock solution is 100 mM in DMSO) and this solution is allowed to sit for 4 hours at 4°C. Cryopreserved crystals are used to collect diffraction data on beamline X8C at the National Synchrotron Light Source at Brookhaven National Laboratory.
Cell Research	Cell lines: Three wild-type p53 (HCT116,RKO,and SJSA1) and 2 mutant p53 (SW480 and MDA-MB-435) cell lines. Concentrations: ~5 μM. Incubation Time: 5 d. Method: Cell proliferation/viability is evaluated by the tetrazolium dye (MTT) assay.Cell growth kinetics are measured using the IncuCyte live cell imaging system.For cell-cycle analysis, cells are cultured in T75 flask with appropriate growth medium (106 cells/condition in 10

Cell Research	mL) and incubated overnight at 37°C.They are incubated with test compounds and processed.
Animal Research	Animal Models: Nude mice bearing SJSA-1,MHMn,or LNCaP xenografts. Formulation: Suspended in 1% Klucel LF/0.1% Tween 80. Dosages: ~200 mg/kg. Administration: p.o.

Solubility Information

Solubility	Ethanol: 93 mg/mL (127.79 mM),Sonication is recommended. DMSO: 250 mg/mL (343.51 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 10 mg/mL (13.74 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	1.374 mL	6.8702 mL	13.7404 mL
5 mM	0.2748 mL	1.374 mL	2.7481 mL
10 mM	0.1374 mL	0.687 mL	1.374 mL
50 mM	0.0275 mL	0.1374 mL	0.2748 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

Vu, Binh; Wovkulich, Peter; Pizzolato, Giacomo et al. Discovery of RG7112: A Small-Molecule MDM2 Inhibitor in Clinical Development. ACS Medicinal Chemistry Letters (2013), 4(5), 466-469.