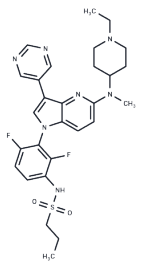
Data Sheet (Cat.No.TQ0048)

TargetMol

BI-882370

Chemical Properties



CAS No. : 1392429-79-6

Formula: C28H33F2N7O2S

Molecular Weight: 569.67

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	BI-882370 is a specific RAF kinase inhibitor. BI-882370 inhibits the oncogenic BRAFV600E-mutant, the WT BRAF and CRAF kinases (IC50s: 0.4, 0.8 and 0.6 nM). BI-882370 also inhibits SRC family kinases.
Targets(IC50)	Raf
In vitro	BI-882370 (0.9-6000 nM; 3 days) inhibits proliferation of BRAF-mutant human melanoma and colorectal cancer cells (EC50: 1-10 nM). BI 882370 (0.1-100 nM, 0.1-3000 nM; 2 hours) reduces p-MEK1/2, p-ERK1/2, and cyclin D1/D2 expression in BRAFV600E-mutant A375 cells and induces phosphorylation of MEK1/2 and enhances phosphorylation of ERK1/2 in WT BRO cells (3-300 nM). BI 882370 (0.1-100 nM, 0.1-3000 nM; 24 hours) suppresses cyclin D1/D2 expression and induces Kip1/p27 expression at concentrations of 1 nM or higher in BRAFV600E-mutant A375 cells, with no effect on expression of cyclins D1/D2 or Kip1/p27 in WT BRO cells.
In vivo	BI-882370 (deliver orally; 25 mg/kg, 50 mg/kg; twice daily; 2 weeks) demonstrates efficacy in mouse models of BRAF-mutant melanomas and colorectal carcinomas, surpassing Vemurafenib, Dabrafenib, or Trametinib. BI-882370 (p.o; 25 mg/kg; twice daily; 40 days) develops resistance within 3 weeks, but no resistance is observed during a 5-week second-line therapy with trametinib. BI-882370 (deliver orally; 60 mg/kg; once daily; 2 weeks) exhibits no toxicity in clinical chemistry, hematology, pathology, and toxicogenomics in rats.
Cell Research	Cell Line: BRAF-mutant and WT melanoma cell lines (A101D, A375, SK-MEL-28, G-361, and BRO); Colorectal cancer cell lines (COLO 205, HT-29, LS411N, and HCT-116). Concentration: 0.9-6000 nM. Incubation Time: 3 days
Animal Research	Animal Model: Human melanoma xenografts in nude mice with BRAF-mutant melanomas and colorectal carcinomas cells (A375, COLO 205; G-361, HT-29 cells). Dosage: 25 mg/kg; 50 mg/kg. Administration: Deliver orally; 25 mg/kg, 50 mg/kg; twice daily; 2 weeks

Solubility Information

Solubility	DMSO: 5 mg/mL (8.78 mM),Sonication and heating to 60°C are recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 1 mg/mL (1.76 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	1.7554 mL	8.777 mL	17.554 mL
5 mM	0.3511 mL	1.7554 mL	3.5108 mL
10 mM	0.1755 mL	0.8777 mL	1.7554 mL
50 mM	0.0351 mL	0.1755 mL	0.3511 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

Waizenegger IC, et al. A Novel RAF Kinase Inhibitor with DFG-Out-Binding Mode: High Efficacy in BRAF-Mutant Tumor Xenograft Models in the Absence of Normal Tissue Hyperproliferation. Mol Cancer Ther. 2016 Mar;15(3): 354-65.