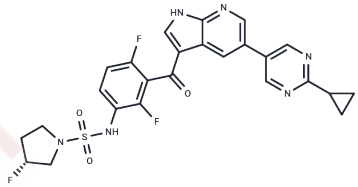
Data Sheet (Cat.No.T3579)

TargetMol

PLX8394

Chemical Properties



CAS No. : 1393466-87-9

Formula: C25H21F3N6O3S

Molecular Weight: 542.53

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	Plixorafenib (PLX8394) is an orally active inhibitor of the serine/threonine protein kinase B-Raf (BRAF) protein.Plixorafenib can selectively bind to and inhibit the activity of wild-type and mutant forms of BRAF, inhibiting the proliferation of tumor cells expressing mutant forms of BRAF.
Targets(IC50)	Raf
In vitro	**METHODS**: Parental 1205LuTR reporter cells and PRT#3 and #4 were treated with Plixorafenib (PLX8394) (1 μM, 24 hours), then cells were lysed and analyzed by western blot for the indicated cyclins; 1205Lu, PRT #3, and PRT #4 were treated with (PLX8394) (1 μM, 24 hours), EdU was added for the last 16 hours, and EdU incorporation was analyzed by flow cytometry. **RESULTS** Plixorafenib effectively reduced the expression of cyclin D3 and cyclin D1, phosphorylated retinoblastoma protein, and cyclin A2 in parental 1205Lu cells; no reduction was observed in PRT #3 and PRT #4 cells; Plixorafenib inhibited EdU incorporation during the S phase in PRT #3 and PRT #4 cells. [1]
In vivo	**METHODS**: Plixorafenib (PLX8394) (75, 150, 300 mg/kg, oral) was treated in HCC364 cell model mice, and serum concentrations (ng/mL) were measured at 0, 1, 2, 4, and 8 hours after treatment; HCC364 cells stably expressing firefly luciferase were surgically implanted into immunodeficient mice, and mice were treated with plixorafenib (150 mg/kg, oral) and tumor growth and response to RAF inhibitor treatment were monitored using a bioluminescence imaging (BLI) system. **RESULTS** Plixorafenib (150 mg/kg) produced plasma concentrations >150μM without significant toxicity to the animals; Plixorafenib significantly inhibited tumor growth, and a more rapid and substantial initial antitumor response was observed in the treatment, an effect associated with enhanced and sustained inhibition of ERK phosphorylation and tumor cell proliferation. [2]
Cell Research	Dissolvent: DMSO. For MTT assays, 2×103?cells are seeded in triplicate in 96 wells in their regular culture medium (containing PLX4720 for PRT lines). Next day, cells are washed twice with PBS and then the medium is replenished containing the indicated RAF inhibitor. Medium is changed 48 hours later and after a further 48 hours, 10 μL of 5 mg/mL MTT reagent is added to wells and incubated for three hours. Formazan crystals are then solubilized overnight with a 1:10 dilution of 0.1 M glycine (pH 10.5) in DMSO. Wells are then analyzed at 450 nM in a Multiskan Spectrum spectrophotometer. Results depicted are normalized to DMSO conditions and are a composite of three independent

Cell Research	experiments. Error bars shown are representative of the standard error of mean (SEM).
Animal Research	PLX8394 is dissolved in PEG 400 [20% (v/v)], TPGS [5% (v/v)], and water [75% (v/v)]. H1755 tumor xenografts are generated by injection of 5×106 cells in a 50/50 mixture for matrigel and PBS into 6- to 8-wk-old female NOD/SCID mice. Mice are randomized to treatment groups once tumors reach an average size of 150 mm3. H1755 cells are s.c. implanted and allowed to grow to appr 200 mm3 (4 wk after implantation). Mice are then treated with vehicle, vemurafenib, or PLX8394 for 15 d. The vehicle for daily oral gavage is PEG 400 [20% (vol/vol)], tocopheryl polyethylene glycol succinate (TPGS) [5% (vol/vol)], water [75% (vol/vol)]. PLX8394 is dissolved in PEG 400 [20% (vol/vol)], TPGS [5% (vol/vol)], and water [75% (vol/vol)] and vortexed continuously throughout the dosing period. PLX8394 (p.o.) is given at a dose of 150 mg/kg/d.

Solubility Information

Solubility	DMSO: 50 mg/mL (92.16 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 (3.69 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	1.8432 mL	9.2161 mL	18.4322 mL
5 mM	0.3686 mL	1.8432 mL	3.6864 mL
10 mM	0.1843 mL	0.9216 mL	1.8432 mL
50 mM	0.0369 mL	0.1843 mL	0.3686 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

Basile KJ, et al. Inhibition of mutant BRAF splice variant signaling by next-generation, selective RAF inhibitors. Pigment Cell Melanoma Res. 2014 May;27(3):479-84.
Okimoto RA, et al. Preclinical efficacy of a RAF inhibitor that evades paradoxical MAPK pathway activation in protein kinase BRAF-mutant lung cancer. Proc Natl Acad Sci U S A. 2016 Nov 22;113(47):13456-13461.

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