Product Data Sheet

Product Name: PLX8394
Cat. No.: GC32686

Chemical Properties

Cas. No.	1393466-87-9		
SMILES	O=C(C1=C(F)C(NS(=O)(N2CC[C@@H](F)C2)=O)=CC=C1F)C3=CNC4=C3C=C(C=N4)C5=CN=C(C6CC6)N=C5		
Formula	$C_{25}H_{21}F_3N_6O_3S$	M.Wt	542.53
Solubility	DMSO : ≥ 39 mg/mL (71.89 mM);Water : < 0.1 mg/mL (insoluble)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	PLX8394		

Protocol

Cell experiment:

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 experiments. Error bars shown are representative of the standard error of mean (SEM).

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Animal experiment:

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, PLX4032, 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 is given daily by oral gavage at a dose of 150 mg/kg/d.

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References:

[1]. 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):479-484.
[2]. 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

Background

PLX8394 is a next-generation, orally available, small-molecule BRAF inhibitor with IC50 values of 3.8 nM, 14 nM and 23 nM for BRAF(V600E), WT BRAF and CRAF respectively. It has potential antineoplastic activity.

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PLX8394 is a next-generation, orally available small-molecule BRAFi that does not induce the RAF/MEK/ERK paradoxical activation and blocks signaling from both monomeric BRAFV600 and dimeric BRAFnon-V600 protein[1].

[1] Filip Janku, et al. AACR Mol Cancer Ther. 2018, 17(1 Suppl): Abstract nr B176. [2] Zhang C, et al. Nature. 2015, 526(7574):583-6. [3] Tutuka CSA, et al. Mol Cancer. 2017, 16(1):112.

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