Vemurafenib

Cat. No.: HY-12057

CAS No.: 918504-65-1

Molecular Formula: $C_{23}H_{18}ClF_2N_3O_3S$

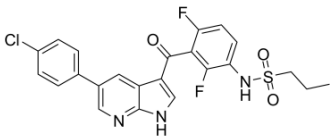
Molecular Weight: 489.92

Target: Raf; Autophagy

Pathway: MAPK/ERK Pathway; Autophagy

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (102.06 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0411 mL	10.2057 mL	20.4115 mL
5 mM	0.4082 mL	2.0411 mL	4.0823 mL
10 mM	0.2041 mL	1.0206 mL	2.0411 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.25 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.25 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Vemurafenib (PLX4032) is a first-in-class, selective, potent inhibitor of B-RAF kinase, with IC_{50}s of 31 and 48 nM for RAF^{V600E} and c-RAF-1, respectively[1][4]. Vemurafenib induces cell autophagy[5].

IC_{50} & Target

B-Raf^{V600E}	c-Raf-1
31 nM (IC_{50})	48 nM (IC_{50})

In Vitro

Vemurafenib (PLX4032) selectively blocks the RAF/MEK/ERK pathway in BRAF mutant cells[1]. RG7204 is a potent inhibitor of proliferation in those expressing RAF^{V600E} but not $BRAF^{WT}$ in 17 melanoma cell lines. Vemurafenib (RG7204) induces MEK and ERK phosphorylation at high concentrations in CHL-1 cells[2]. Ectopic expression of EGFR in melanoma cells is sufficient

	to cause resistance to PLX4032[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Vemurafenib (PLX4032, 20, 25, 75 mg/kg, p.o.) causes dose-dependent inhibition of tumor growth, with higher exposures resulting in tumor regression of BRAF mutant xenografts[1]. RG7204 (12.5, 25, and 75 mg/kg, p.o.) significantly inhibits tumor growth and induced tumor regression in mice bearing LOX tumor xenografts[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Briefly, cells are plated in 96-well microtiter plates at a density of 1,000 to 5,000 cells per well in a volume of 180 µL. For the assay, Vemurafenib (RG7204) is prepared at 10 times the final assay concentration in media containing 1% DMSO. Twenty-four hours after cell plating, 20 µL of the appropriate dilution are added to plates in duplicate. The plates are assayed for proliferation 6 days after the cells are plated according to the procedure. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Athymic nude mice, are with ages 13 to 14 weeks, and weighing approximately 23 to 25 g. For the LOX xenografts, 2×10^6 cells in 0.2 mL of PBS are injected s.c. into the right lateral flank. Vemurafenib (RG7204), formulated as MBP, is suspended at the desired concentration as needed for each dose group in an aqueous vehicle containing 2% Klucel LF and adjusted to pH 4 with dilute HCl. NSC 362856 is of 250-mg capsules. Capsules are opened and combined into one bulk supply. To prepare the stock dosing material, NSC 362856 is first dissolved in 100% DMSO followed by dilution with saline to form a final milky white suspension in 10% DMSO/90% saline (pH 3.4). MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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CUSTOMER VALIDATION

- Cell Res. 2020 Oct;30(10):833-853.
- Nat Biomed Eng. 2018;2:578-588.
- Sci Transl Med. 2018 Jul 18;10(450). pii: eaaq1093.
- Sci Adv. 2019 Aug 14;5(8):eaav8463.
- Nat Commun. 2015 Sep 24;6:8390.

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REFERENCES

[1]. Bollag G, et al. Clinical efficacy of a RAF inhibitor needs broad target blockade in BRAF-mutant melanoma. Nature, 2010, 467(7315), 596-599.

[2]. Yang H, et al. RG7204 (PLX4032), a selective BRAFV600E inhibitor, displays potent antitumor activity in preclinical melanoma models. Cancer Res, 2010, 70(13), 5518-5527.

[3]. Prahallad A, et al. Unresponsiveness of colon cancer to BRAF(V600E) inhibition through feedback activation of EGFR. Nature, 2012, 483(7387), 100-103.

[4]. Shelledy L, et al. Vemurafenib: First-in-Class BRAF-Mutated Inhibitor for the Treatment of Unresectable or MetastaticMelanoma. J Adv Pract Oncol. 2015 Jul-Aug;6(4):361-5.

[5]. Wang W, et al. Targeting Autophagy Sensitizes BRAF-Mutant Thyroid Cancer to Vemurafenib.J Clin Endocrinol Metab. 2017 Feb 1;102(2):634-643.