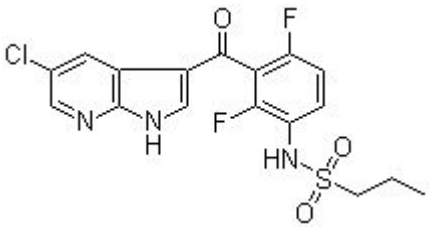
Product Introduction

PLX-4720

PLX4720 is a potent and selective inhibitor of **B-Raf^{V600E}** with **IC50** of 13 nM, equally potent to c-Raf-1(Y340D and Y341D mutations), 10-fold selectivity for B-RafV600E than wild-type B-Raf.

Technical Data:

Molecular Weight (MW):	413.83	
Formula:	$C_{17}H_{14}ClF_2N_3O_3S$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 83 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	918505-84-7	

Biological Activity

PLX-4720 displays >10 times selectivity against wild type B-Raf, and >100 times selectivity over other kinases such as Frk, Src, Fak, FGFR, and Aurora A with IC50 of 1.3-3.4 μM. PLX-4720 significantly inhibits the ERK phosphorylation in cell lines bearing B-Raf^{V600E} with IC50 of 14-46 nM, but not the cells with wild-type B-Raf. PLX-4720 significantly inhibits the growth of tumor cell lines bearing the B-Raf^{V600E} oncogene, such as COLO205, A375, WM2664, and COLO829 with GI50 of 0.31 μM, 0.50 μM, 1.5 μM, and 1.7 μM, respectively. In addition, PLX-4720 treatment at 1 μM induces cell cycle arrest and apoptosis

exclusively in the B-Raf^{V600E}-positive 1205Lu cells, but not in the B-Raf wild-type C8161 cells. [1] PLX-4720 treatment (10 μM) significantly induces >14-fold expression of BIM in the PTEN^{+} cells, compared with the PTEN- cell lines (4-fold), giving an explanation of the resistance of PTEN^{-} cells to PLX-4720-induced apoptosis. [2]

Oral administration of PLX-4720 at 20 mg/kg/day induces significant tumor growth delays and regressions in B-Raf^{V600E}-dependent COLO205 tumor xenografts, without obvious adverse effects in mice even at dose of 1 g/kg. PLX-4720 at 100 mg/kg twice daily almost completely eliminates the 1205Lu xenografts bearing B-Raf^{V600E}, while has no activity against C8161 xenografts bearing wild-type B-Raf. The anti-tumor effects of PLX-4720 correlate with the blockade of MAPK pathway in those cells harboring the V600E mutation. [1] PLX-4720 treatment at 30 mg/kg/day significant inhibits the tumor growth of 8505c xenografts by >90%, and dramatically decreases distant lung metastases. [3]

References

[1] Tsai J, et al. Proc Natl Acad Sci U S A, 2008, 105(8), 3041-3046.

[2] Paraiso KH, et al. Cancer Res, 2011, 71(7), 2750-2760.

[3] Nucera C, et al. Proc Natl Acad Sci U S A, 2010, 107(23), 10649-10654.

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