For Research Use Only

PLX-4720

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Catalog Number: CM06265

产品信息

Catalog Number:
CM06265

CAS号:
918505-84-7

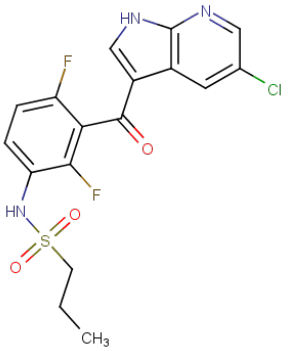
分子式:
$C_{17}H_{14}ClF_2N_3O_3S$

主要靶点:
Raf

主要通路:
MAPK信号通路

分子量:
413.83

溶解度:
Ethanol:<1 mg/mL,H2O:<1 mg/mL,DMSO:77 mg/mL (186.1 mM)



靶点活性

B-Raf:160 nM (cell free)|B-Raf (V600E):13 nM (cell free)|c-Raf-1 (Y340D/Y341D):6.7 nM (cell free)

体外活性

PLX4720 inhibits B-Raf(V600E) with an IC50 of 13 nM. Consistent with the high degree of selectivity, ERK phosphorylation is potently inhibited by PLX4720 in B-Raf(V600E)-bearing tumor cell lines but not in cells lacking oncogenic B-Raf [1]. PLX4720 treatment significantly increased BIM expression in the PTEN+ (>14-fold) compared with the PTEN- cell lines (four-fold). Dual treatment of PTEN- cells with PLX4720 and a PI3K inhibitor enhanced BIM expression at both the mRNA and protein level and increased the level of apoptosis through a mechanism involving AKT3 and the activation of FOXO3a [2].

体内活性

In B-Raf(V600E)-dependent tumor xenograft models, orally dosed PLX4720 causes significant tumor growth delays, including tumor regressions, without evidence of toxicity [1]. In vivo, PLX4720 treatment of 8505c orthotopic thyroid tumors inhibited tumor aggressiveness and significantly upregulated the thyroid differentiation markers thyroid transcription factor 1 and paired box gene 8 [3]. Treatment of orthotopic thyroid tumors, initiated 1 week after tumor cell implantation with PLX4720 caused a significant tumor growth delay and decreased distant metastases, without evidence of toxicity [4].

动物实验

Female athymic mice (NCr nu/nu) were implanted s.c. on day 0 with 30–60 mg COLO205 tumor fragments. Treatments began on day 11, when the mean estimated tumor mass was 104 mg (range, 95–113 mg). All animals were dosed with vehicle (5% DMSO, 1% methylcellulose) or PLX4720 suspended in vehicle by gavage daily for 14 consecutive days. Tumor burden (mg) was estimated from caliper measurements [1].

细胞实验

Cells are treated with various concentrations PLX-4720 for 24, 48, and 72 hours. Cell proliferation is measured by using the CellTiter-Glo Luminescent Cell Viability Assay or MTT assay. For cell cycle analysis, supernatant and cells are collected, pelleted, and fixed with 70% ethanol. Before staining with propidium iodide (10 μg/mL), cells are incubated for 1 hour at 37 °C in 0.5 mg/mL RNase I to rid samples of residual RNA contamination. Samples are then analyzed by using the EPICS XL apparatus. For the assessment of apoptosis, media and cells are harvested and pelleted before staining with annexin-FITC and propidium iodide. Samples are subsequently analyzed by using the EPICS XL apparatus [1].

描述

PLX-4720 is a potent and selective inhibitor of B-Raf (V600E) (IC50: 13 nM), equally potent to c-Raf-1(Y340D and Y341D mutations).

储存

Powder: -20°C for 3 years | In solvent: -80°C for 2 years

For technical support and original validation data for this product please contact
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