NVP-BAW2881

Cat. No.: HY-100394

CAS No.: 861875-60-7

Molecular Formula: $C_{22}H_{15}F_3N_4O_2$

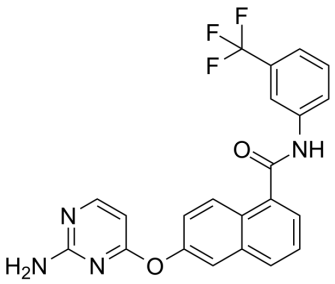
Molecular Weight: 424.38

Target: VEGFR

Pathway: Protein Tyrosine Kinase/RTK

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 : ≥ 33 mg/mL (77.76 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3564 mL	11.7819 mL	23.5638 mL
5 mM	0.4713 mL	2.3564 mL	4.7128 mL
10 mM	0.2356 mL	1.1782 mL	2.3564 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: ≥ 2.5 mg/mL (5.89 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.89 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

NVP-BAW2881 (BAW2881) is a potent and selective VEGFR2 inhibitor with an IC_{50} of 4 nM.

IC_{50} & Target

VEGFR1	VEGFR2	VEGFR3
820 nM (IC_{50})	9 nM (IC_{50})	420 nM (IC_{50})

In Vitro

The VEGF-driven cellular receptor autophosphorylation in CHO cells of BAW2881 is inhibited with an IC_{50} of 4 nM. BAW2881 inhibits a limited number of kinases including c-RAF, B-RAF, RET, ABL, and TIE-2 at sub-μM IC_{50}s[1]. NVP-BAW2881 is highly selective for VEGFR, although it also demonstrates activity against Tie2 (IC_{50}=650 nM) and RET (IC_{50}=410 nM). The IC_{50} values of NVP-BAW2881 toward a wide panel of other kinases are >10 μM. NVP-BAW2881 inhibits VEGF-A-induced phosphorylation

	of VEGFR-2 in HUVECs and in VEGFR-2-transfected Chinese hamster ovary cells, with IC_{50} values of 2.9 and 4.2 nM, respectively[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In a transgenic mouse model of psoriasis, NVP-BAW2881 reduces the number of blood and lymphatic vessels and infiltrating leukocytes in the skin, and normalized the epidermal architecture. NVP-BAW2881 also displays strong anti-inflammatory effects in models of acute inflammation; pretreatment with topical NVP-BAW2881 significantly inhibits VEGF-A-induced vascular permeability in the skin of pigs and mice[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	HUVECs or LECs (1200) are seeded into fibronectin-coated 96-well plates. After 24 hours, the cells are transferred into LEC medium containing 2% fetal bovine serum and incubated for an additional 24 hours. Cells (eight wells/condition) are incubated with medium alone (control), 20 ng/mL VEGF-A, or a combination of 20 ng/mL VEGF-A and 1 nM to 1 μM NVP-BAW2881. Proliferation is also assayed in LECs incubated with 500 ng/mL VEGF-C. The DMSO is adjusted to 0.1% in all wells. After 72 hours, cells are incubated with 5-methylumbelliferylheptanoate for subsequent fluorescent quantification of viable cells, using a electron microscope[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice: A contact hypersensitivity response is induced in the ear skin of 8-week-old female K14/VEGF-A TG mice. Five days after sensitization (day 0), the right ear is challenged by topical application of 10 μL oxazolone (1%) on each side. Starting on day 7, once-daily oral doses of 25 mg/kg NVP-BAW2881 or twice-daily topical doses of 0.5% NVP-BAW2881 are administered for 14 days. Control groups are given vehicles alone. The ear thickness is measured every other day using calipers. On day 21, mice are sacrificed and the weight of each ear and of its draining retro-auricular lymph node (LN) is determined[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Bold G, et al. A Novel Potent Oral Series of VEGFR2 Inhibitors Abrogate Tumor Growth by Inhibiting Angiogenesis. J Med Chem. 2016 Jan 14;59(1):132-46.

[2]. Halin C, et al. Inhibition of chronic and acute skin inflammation by treatment with a vascular endothelial growth factor receptor tyrosine kinase inhibitor. Am J Pathol. 2008 Jul;173(1):265-77.

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