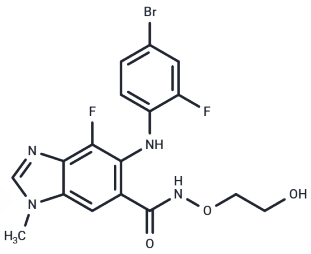
Data Sheet (Cat.No.T2508)

TargetMol

Binimetinib

Chemical Properties



CAS No. : 606143-89-9

Formula: C17H15BrF2N4O3

Molecular Weight: 441.23

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Binimetinib (ARRY-162) is a MEK1/2 inhibitor (IC50=12 nM) with selective and oral activity. Binimetinib has antitumor activity for the treatment of metastatic melanoma that cannot be resected or has a BRAF V600E or V600K mutation.
Targets(IC50)	MEK,Autophagy
In vitro	In models of collagen-induced arthritis (CIA) and adjuvant-induced arthritis (AIA) in rats, ARRY-438162 demonstrated significant anti-inflammatory effects. At doses of 1/3 mg/kg administered twice daily orally (p.o.), ARRY-438162 reduced ankle diameter swelling by 27%/50% in the CIA model, outperforming ibuprofen's 46% reduction. Higher doses of 3/10 mg/kg showed 11%/34% inhibition of ankle swelling in the AIA model. Moreover, in immunodeficient mice injected with MCF7-RSK4 cells, the combination of ARRY-438162 (6 mg/kg, twice daily) with BEZ235 significantly diminished tumor growth. In the AIA rat model, ARRY-438162 (10 mg/kg) completely suppressed serum IL-6 concentrations in a dose-dependent manner compared to controls. Similarly, in both CIA and AIA rat models, administration of ARRY-438162 (10 mg/kg, twice daily p.o.) dose-dependently ameliorated disease severity. The same dosing regimen significantly mitigated lesions (inflammation, cartilage damage, angiogenesis, and bone resorption) in the CIA model, with 1/3 mg/kg doses inhibiting these effects by 32% and 60%, respectively. Furthermore, in the AIA rat model, ARRY-438162 at 10/30 mg/kg doses significantly and dose-dependently reduced ankle swelling compared to control groups.
In vivo	ARRY-438162 is an ATP non-competitive inhibitor for MEK1/2, capable of inhibiting intracellular pERK with an IC50 of 11 nM. When used in combination, MEK162 (1 μM) and MK-2206 (2 μM) can fully reverse the resistance of MCF7 cells expressing RSK. ARRY-438162 at 2 μM exhibits minimal impact on osteoblast differentiation. At a concentration of 10 μM, ARRY-438162 inhibits osteoclast resorption in vitro with an IC50 of 625 nM. Additionally, ARRY-438162 at 625 nM suppresses osteoclast differentiation in vitro with an IC50 of 39 nM.
Cell Research	MEK162 is dissolved in DMSO and stored, and then diluted with appropriate medium before use[2]. MCF7 cells infected as indicated are seeded in 12-well plates (2×104). After 24 hours, cells are treated with BEZ235 (100 or 200 nM), BKM120 (0.75 or 1 μM), GDC-0941 (1 μM), or MK2206 (2 μM) alone or in combination with MEK162 (1 μM), BI-D1870 (10 μM), or AZD6244 (1 μM), as indicated in text. Cell numbers are quantified by fixing cells with 4% glutaraldehyde or methanol, washing the cells twice in Water, and staining the cells with 0.1% crystal violet. The dye is subsequently extracted with 10%

Cell Research	acetic acid, and its absorbance is determined (570 nm). Growth curves are performed in triplicate. Viability assays with CellTiter-Glo are performed by plating 2,000 cells in 96-well plates, adding the drug at 24 hours, and assaying 4 to 5 days after drug addition. Cell-cycle and hypodiploid apoptotic cells are quantified by flow cytometry. Briefly, cells are washed with PBS, fixed in cold 70% ethanol, and then stained with propidium iodide while being treated with RNase. Quantitative analysis of sub-G1 cells is carried out in a FACScalibur cytometer using Cell Quest software[2].

Solubility Information

Solubility	DMSO: 50 mg/mL (113.32 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (4.53 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2664 mL	11.332 mL	22.6639 mL
5 mM	0.4533 mL	2.2664 mL	4.5328 mL
10 mM	0.2266 mL	1.1332 mL	2.2664 mL
50 mM	0.0453 mL	0.2266 mL	0.4533 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Woodfield SE, et al. Binimetinib inhibits MEK and is effective against neuroblastoma tumor cells with low NF1 expression. BMC Cancer. 2016 Mar 1;16:172.
Fan K, Ni X, Shen S, et al. Acetylation stabilizes stathmin1 and promotes its activity contributing to gallbladder cancer metastasis. Cell Death Discovery. 2022, 8(1): 1-13
Yao W, et al. Enhancing therapeutic efficacy of the MEK inhibitor, MEK162, by blocking autophagy or inhibiting PI3K/Akt signaling in human lung cancer cells. Cancer Lett. 2015 Aug 1;364(1):70-8.
SS Bhagwat, et al. Annu Rep Med Chem, 2007, 42, 265-278.
Serra V, et al. J Clin Invest, 2013, 123(6), 2551-2563.
Cheng H, et al. PIK3CA(H1047R)- and Her2-initiated mammary tumors escape PI3K dependency by compensatory activation of MEK-ERK signaling. Oncogene. 2016 Jun 9;35(23):2961-70.
Seip K, et al. Fibroblast-induced switching to the mesenchymal-like phenotype and PI3K/mTOR signaling protects melanoma cells from BRAF inhibitors. Oncotarget. 2016 Apr 12;7(15):19997-20015.

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