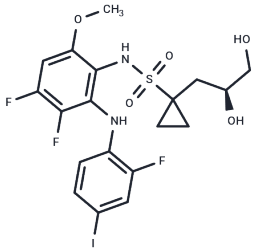
Data Sheet (Cat.No.T6636)

TargetMol

Refametinib

Chemical Properties



CAS No. : 923032-37-5

Formula: C19H20F3IN2O5S

Molecular Weight: 572.34

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	Refametinib (RDEA119) (RDEA119, Bay 86-9766) is an effective, ATP non-competitive and specific inhibitor of MEK1/2 (IC50: 19/47 nM).
Targets(IC50)	MEK
In vitro	RDEA119 is selectively bound directly to an allosteric pocket in the MEK1/2 enzymes, and highly efficacious at inhibiting cell proliferation in several tumor cell lines, including A375, SK-MEI-28, Colo205, HT-29 and BxPC3. RDEA119 inhibits anchorage-dependent growth of human cancer cell lines harboring the gain-of-function V600E BRAF mutant with GI50 values ranging from 67 to 89 nM. Under anchorage-independent conditions, GI50 values for all cell lines tested are similar (40-84 nM). RDEA119 shows a tissue selectivity that reduces its potential for central nervous system-related side effects. [1] RDEA119 potently inhibits the proliferation of the 4 cell lines that harbored BRAF mutation but has no or modest effects on the other 4 cells that harbored wild-type BRAF (IC50 of 0.034-0.217 μM vs. 1.413-34.120 μM). This inhibitory effect of RDEA119 in selected cell lines OCUT1 (BRAF V600E(+), PIK3CA H1047R(+)) and SW1376 (BRAF V600E (+)) is enhanced by combination with the mTOR inhibitor, temsirolimus. RDEA119 and temsirolimus also show synergistic effects on autophagic death of OCUT1 and KAT18 cells selectively tested. [2]
In vivo	Oral administration of RDEA119 at 50 mg/kg on a once daily x 14 schedule leads to a 68% tumor growth inhibition (TGI) in human melanoma A375 tumor model. Oral administration of RDEA119 at 25 mg/kg on a once a once daily x 14 schedule leads to a 123% TGI in human colon carcinoma Colo205 tumor model (TGI > 100% occurs when the tumor shrinks below its starting volume). A dose of 25 mg/kg once daily x 14 produces 56% and 67% TGI for HT-29 and A431 tumors, respectively. [1]
Kinase Assay	MEK Kinase Assay: Kinase inactive murine ERK2 (mERK2) K52A/T183A is affinity purified from Escherichia coli expressed using the pET21a vector. MEK1 kinase activity is determined using mERK2 K52A T183A as the substrate. Recombinant MEK1 enzyme (5 nM) is first activated by 0.02 unit or 1.5 nM of RAF1 in the presence of 25 mM HEPES (pH 7.8), 1 mM MgCl2, 50 mM NaCl, 0.2 mM EDTA, and 50 μM ATP for 30 minutes at 25 °C. The reactions are initiated by adding 2 μM of mERK2K52A T183A and 2.5 μCi [γ-33P] ATP in a total volume of 20 μL. The MEK2 kinase activity is determined similarly except that activation by RAF1 is not needed and 11 nM of MEK2 enzyme (active) are used in the assays.Kinase profiling is performed by Invitrogen using their Select Screen Kinase

Kinase Assay	Profiling Service. The Z'-LYTE biochemical assay is used. RDEA119 is assayed in quadruplicate at 10 μM against 205 kinases.
Cell Research	For anchorage-dependent growth inhibition experiments, cells are plated in white 384-well plates at 1,000/20 μL/well or white 96-well microplates at 4,000/100 μL/well. After 24-h incubation at 37 °C, 5% CO2, and 100% humidity, RDEA119 is incubated for 48 hours at 37 °C and assayed using CellTiter-Glo. For the 96-well anchorage-independent growth assay, wells of an "ultralow binding" plate (Corning) are filled with 60 μL of a 0.15% agarose solution in complete RPMI 1640. Then, 60 μL of complete RPMI 1640 containing 9,000 cells in 0.15% agarose are added per well. After 24 hour, 60 μL of a 3 × drug solution in agarose-free complete RPMI 1640 are added. After 7 d, 36 μL of 6 × 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)- 2H-tetrazolium, inner salt reagent are added per well. After 2 hours at 37 °C, absorbance at 490 nm is determined on the M5 plate reader. (Only for Reference)

Solubility Information

Solubility	Ethanol: 93 mg/mL (162.49 mM),Sonication is recommended. DMSO: 150 mg/mL (262.08 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.7472 mL	8.7361 mL	17.4721 mL
5 mM	0.3494 mL	1.7472 mL	3.4944 mL
10 mM	0.1747 mL	0.8736 mL	1.7472 mL
50 mM	0.0349 mL	0.1747 mL	0.3494 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

Iverson C, et al, Cancer Res, 2009, 69(17), 6839-6847.
Liu D, et al, Int J Cancer, 2010, 127(12), 2965-2973.
Li Y, He Y, Peng J, et al. Mutant Kras co-opts a proto-oncogenic enhancer network in inflammation-induced metaplastic progenitor cells to initiate pancreatic cancer[J]. Nature Cancer. 2020: 1-17.

Tel:781-999-4286 E_mail:info@targetmol.com Address:34 Washington Street,Wellesley Hills,MA 02481