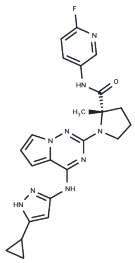
Data Sheet (Cat.No.T2349)

TargetMol

BMS-754807

Chemical Properties



CAS No. : 1001350-96-4

Formula: C23H24FN9O

Molecular Weight: 461.49

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	Dual IGF-1R/InsR Inhibitor BMS-754807 is an oral small molecule inhibitor of insulin-like growth factor 1 receptor (IGF-1R) and insulin receptor (InsR) tyrosine kinases with potential antineoplastic activity.
Targets(IC50)	c-Met/HGFR,IGF-1R,Trk receptor
In vitro	MS-754807 (6.25 mg/kg) achieved complete tumor growth inhibition in a transgenic-derived IGF-Sal tumor model in mice, while simultaneously inhibiting associated pIGF-1R and pAKT. In nude mice with IGF-1R-Sal tumors, BMS-754807 (12.5 mg/kg, orally) inhibited tumor and serum IGF-1R phosphorylation. At a dose of 25 mg/kg, BMS-754807 significantly inhibited tumor growth in mouse models carrying KT-5 (Wilms), KT-14 (rhabdoid), Rh28 (rhabdomyosarcoma), and OS-1 xenografts. Furthermore, BMS-754807 effectively suppressed tumor growth across a selection of epithelial (IGF-1R-Sal, GEO, and Colo205), hematopoietic (JJN3), and mesenchymal (RD1 and Rh41) xenograft models, with tumor growth inhibition rates ranging from 53% to 115%.
In vivo	BMS-754807 inhibits the phosphorylation of IGF-1R in IGF-1R-Sal cells, Rh41, and Geo with IC50 values of 13 nM, 6 nM, and 21 nM, respectively. It similarly inhibits the phosphorylation of Akt in these cells, with IC50 values of 22 nM, 13 nM, and 16 nM. Additionally, BMS-754807 induces apoptosis in Rh41 cells and suppresses the proliferation of IGF-1R-Sal and Rh41 cells, with IC50 values of 7 nM and 5 nM, respectively. In the pediatric preclinical testing program (PPTP), BMS-754807 exhibited activity across 23 cell lines with an average EC50 value of 0.62 μM, covering a range of cell types including mesenchymal (Ewing's, rhabdomyosarcoma, neuroblastoma, and liposarcoma), epithelial (breast, lung, pancreatic, colon, and gastric cancers), and hematopoietic stem cells (multiple myeloma and leukemia), with IC50 values spanning from 5 nM to 365 nM.
Kinase Assay	Kinase inhibition assays: The primary screen for BMS-754807 is an in vitro kinase assay using recombinant human IGF-1 receptor enzyme in biochemical assays using synthetic peptide KKSRGDYMTMQIG as a phosphoacceptor substrate. The selectivity profile is evaluated against multiple recombinant enzymes that are generated at BMS or purchased externally. The enzymatic assays are performed in Ubottom 384-well plates using a 30 μL reaction volume in assay buffer (100 mM Hepes pH 7.4, 10 mM MgCl2, 0.015% Brij35 and 4 mM DTT). The 60 minute reactions are initiated by combining ATP (concentration equivalent to Km ATP), 1.5 μM fluoresceinlabeled peptide substrate, enzyme and BMS-754807. The reactions are terminated with EDTA. The reaction mixtures

Kinase Assay	are analyzed on the Caliper LabChip 3000 by electrophoretic separation of the fluorescent substrate and phosphorylated product. Inhibition data are calculated by comparison to enzyme-free control reactions for 100% inhibition and vehicle-only reactions for 0% inhibition. Compounds are dissolved in dimethylsulfoxide (DMSO, 10 mM stock) and evaluated at eleven concentrations. IC50 values are derived by non-linear regression analysis of the dose response curves.
Cell Research	Cells are grown at their optimal density in RPMI +GlutaMax supplemented with 10% heat-inactivated fetal bovine serum (FBS), 10 mM Hepes, penicillin, and streptomycin. Cell proliferation is evaluated by incorporation of 3H-thymidine into DNA after exposure of cells to BMS-754807 for 72 hours. Results are expressed as an IC50, which is the drug concentration required to inhibit cell proliferation by 50% compared with untreated control cells.(Only for Reference)

Solubility Information

Solubility	Ethanol: 85 mg/mL (184.19 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 240 mg/mL (520.05 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 10 mg/mL (21.67 mM),Solution. 10% DMSO+90% Saline: < 10 mg/mL (21.67 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. *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	2.1669 mL	10.8345 mL	21.6689 mL
5 mM	0.4334 mL	2.1669 mL	4.3338 mL
10 mM	0.2167 mL	1.0834 mL	2.1669 mL
50 mM	0.0433 mL	0.2167 mL	0.4334 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

Carboni JM, et al. Mol Cancer Ther, 2009, 8(12), 3341-3349.
Wittman MD, et al. J Med Chem, 2009, 52(23), 7360-7363.
Kolb EA, et al. Pediatr Blood Cancer, 2011, 56(4), 595-603.
Silbermann K, Stefan S, Elshawadfy R, et al. Identification of Thienopyrimidine Scaffold as Inhibitor of the ABC Transport Protein ABCC1 (MRP1) and Related Transporters Using a Combined Virtual Screening Approach[J]. Journal of Medicinal Chemistry. 2019.

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