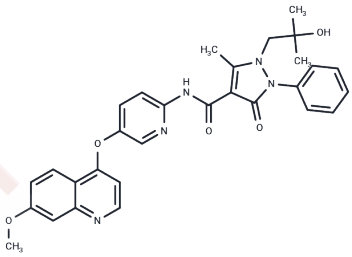
Data Sheet (Cat.No.T6378)

TargetMol

AMG-458

Chemical Properties



CAS No. : 913376-83-7

Formula: C30H29N5O5

Molecular Weight: 539.58

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	AMG-458 is a potent c-Met inhibitor with Ki of 1.2 nM, ~350-fold selectivity for c-Met than VEGFR2 in cells.
Targets(IC50)	c-Met/HGFR
In vitro	AMG 458 also inhibits HGF-mediated c-Met phosphorylation in PC3 and CT26 cells with IC50 of 60 and 120 nM. [1] AMG 458 is observed to bind covalently to liver microsomal proteins from rats and humans in the absence of NADPH. AMG 458 is believed to react with thiol groups in proteins, producing a methoxy quinoline thioether conjugate. [2] A recent study shows that the constitutive phosphorylation of c-Met in H441 is abrogated by AMG 458. The basal and HGF-induced phosphorylation of c-Met in A549 is attenuated by AMG 458. The combination of radiation therapy and AMG 458 treatment is found to synergistically increase apoptosis in the H441 cell line by reduction of p-Akt and p-Erk levels, but not in A549. [3]
In vivo	AMG 458 is metabolically stable in the liver microsomes of mouse, rat, dog, monkey, and human with low intrinsic clearances (Clint: <5, 62, 8, 8, 18 (μL/min)/mg, respectively). When administered orally, AMG 458 achieves remarkably high bioavailability in all species tested. Oral dosing of AMG 458 inhibits HGF-mediated c-Met phosphorylation with an approximate ED90 of 30 mg/kg and an associated plasma exposure of approximately 15 μM at 6 hours. AMG 458 significantly inhibits tumor growth in the NIH3T3/TPR-Met and U-87 MG xenograft models at 30 and 100 mg/kg q.d. and 30 mg/kg b.i.d.with no adverse effect on body weight. [1] High concentrations of AMG 458 in some organs may produce toxicity via oxidative stress. [2]

Solubility Information

Solubility	DMSO: < 1 mg/mL (insoluble or slightly soluble), H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: < 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	1.8533 mL	9.2665 mL	18.5329 mL
5 mM	0.3707 mL	1.8533 mL	3.7066 mL
10 mM	0.1853 mL	0.9266 mL	1.8533 mL
50 mM	0.0371 mL	0.1853 mL	0.3707 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

Liu L, et al. J Med Chem, 2008, 51(13), 3688-3691.
Teffera Y, et al. Chem Res Toxicol, 2008, 21(11), 2216-2222.
Torossian A, et al. Int J Radiat Oncol Biol Phys, 2012, 84(4), e525-531.