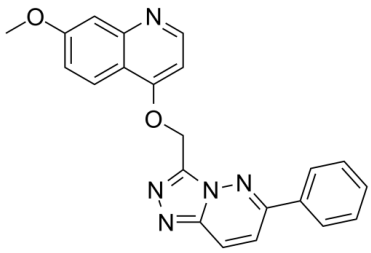
Data Sheet

Product Name:	AMG-208
Cat. No.:	CS-0185
CAS No.:	1002304-34-8
Molecular Formula:	C22H17N5O2
Molecular Weight:	383.40
Target:	c-Met/HGFR
Pathway:	Protein Tyrosine Kinase/RTK
Solubility:	DMSO : 7.8 mg/mL (20.34 mM; Need ultrasonic and warming)



BIOLOGICAL ACTIVITY:

AMG-208 is a potent small molecular c-Met inhibitor with an IC50 of 9.3 nM. IC50 value: 9.3 nM Target: c-Met in vitro: AMG-208 shows the potent inhibition of kinase c-Met activity with IC50 of 9 nM in a cell-free assay. Besides, AMG-208 treatment also leads to the inhibition of HGF-mediated c-Met phosphorylation in PC3 cells with IC50 of 46 nM [1]. Pre-incubation of AMG-208 with human liver microsomes for 30 minutes shows a potent time-dependent inhibition for CYP3A4 metabolic activity with IC50 of 4.1 μM, which is an eightfold decrease relative to the IC50 (32 μM) without preincubation [2]. AMG-208 is identified to be a c-MET and RON dual selective inhibitor [3]. in vivo: In male Sprague Dawley rats, AMG-208 (0.5 mg/kg i.v.) shows a high bioavailability with Cl of 0.37 L/h/kg, Vss of 0.38 L/kg and T1/2 of 1 hour[1].

References:

[1]. Albrecht BK, et al. Discovery and optimization of triazolopyridazines as potent and selective inhibitors of the c-Met kinase. J Med Chem. 2008, 51(10), 2879-2882.

[2]. Boezio AA, et al. Discovery and optimization of potent and selective triazolopyridazine series of c-Met inhibitors. Bioorg Med Chem Lett. 2009, 19(22), 6307-6312.

[3]. Liu X, et al. Developing c-MET pathway inhibitors for cancer therapy: progress and challenges. Trends Mol Med. 2010,16(1), 37-45.

CAIndexNames:

Quinoline, 7-methoxy-4-[(6-phenyl-1,2,4-triazolo[4,3-b]pyridazin-3-yl)methoxy]-

SMILES:

COC1=CC=C2C(OCC3=NN=C4N3N=C(C=C4)C5=CC=CC=C5)=CC=NC2=C1

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