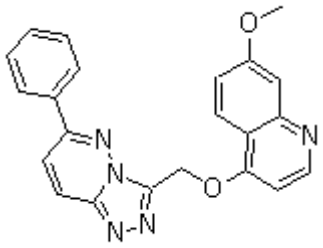
Product Introduction

AMG-208

AMG 208 is a highly selective c-Met inhibitor with IC50 of 9 nM. Phase 1.

Technical Data:

Molecular Weight (MW):	383.4	
Formula:	$C_{22}H_{17}N_5O_2$	
Solubility (25℃) * <1 mg/ml means slightly soluble or insoluble:	DMSO 0.25 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃ Powder	
	6 months-80℃ in DMSO	
CAS No.:	1002304-34-8	

Biological Activity

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] Incubation of AMG-208 with rat and human liver microsomes in the presence of NADPH qualitatively yields C6-phenylarene oxidation products as the major metabolites. [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 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, while AMG-208 (2 mg/kg i.v.) shows a bioavailability with AUC0→∞ of 2517 ng·h/mL and F of 43%, respectively. [1]

References

[1] Albrecht BK, et al. J Med Chem. 2008, 51(10), 2879-2882.

[2] Boezio AA, et al. Bioorg Med Chem Lett. 2009, 19(22), 6307-6312.

[3] Liu X, et al. Trends Mol Med. 2010,16(1), 37-45.