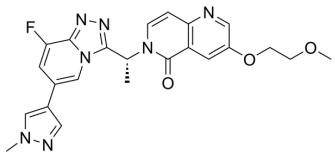
AMG-337

Cat. No.:	HY-18696
CAS No.:	1173699-31-4
Molecular Formula:	$C_{23}H_{22}FN_7O_3$
Molecular Weight:	463.46
Target:	c-Met/HGFR; Caspase; Apoptosis
Pathway:	Protein Tyrosine Kinase/RTK; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (215.77 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1577 mL	10.7884 mL	21.5768 mL
	5 mM	0.4315 mL	2.1577 mL	4.3154 mL
	10 mM	0.2158 mL	1.0788 mL	2.1577 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.39 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.39 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.39 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AMG-337 is a potent, orally active, selective MET kinase inhibitor with IC_{50} values of 1, 1, 4.7, 5, 21.5, 1077 and >4000 nM of WT MET, H1094R MET, M1250T MET, HGF-stimulated pMET (PC3 cells) MET, V1092I MET, Y1230H MET, and D1228H MET, respectively. AMG 337 inhibits the phosphorylation of MET and downstream effectors in MET-amplified cancer cell lines, resulting in an inhibition of MET-dependent cell proliferation and induction of apoptosis[1][2].

IC_{50} & Target

IC_{50}: 1 (WT MET), 1 (H1094R MET), 4.7 (M1250T MET), 5 (HGF-stimulated pMET (PC3 cells) MET), 21.5 (V1092I MET), 1077 (Y1230H MET) and >4000 nM (D1228H MET)[1]

In Vitro

AMG 337 (0-3 μM; 72 h) inhibits proliferation in MET-dependent cancer cell lines[1].
AMG 337 (0-300 nM; 0-24 h; MKN-45, SNU-620, and SNU-5 cells) inhibits signaling through the PI3K and MAPK pathways in MET-amplified gastric cancer cell lines, resulting in an inhibition of MET-dependent cell proliferation and induction of apoptosis[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Apoptosis Analysis[1]

Cell Line:	MKN-45 and SNU-620 cells
Concentration:	0, 3, 10, 30, 100 and 300 nM
Incubation Time:	24 hours
Result:	Increased the number of cells undergoing apoptosis.

Cell Cycle Analysis[1]

Cell Line:	MKN-45 and SNU-620 cells
Concentration:	0, 3, 10, 30, 100 and 300 nM
Incubation Time:	24 hours
Result:	Increased in a dose-dependent in cells in the G1 phase and with concurrent reduction of cells in S-phase.

Western Blot Analysis[1]

Cell Line:	MKN-45, SNU-620, and SNU-5 cells
Concentration:	100 nM
Incubation Time:	2 hours
Result:	Inhibited MET phosphorylation and phosphorylation of downstream effectors.

Western Blot Analysis[1]

Cell Line:	MKN-45, SNU-620, and SNU-5 cells
Concentration:	100 nM
Incubation Time:	24 hours
Result:	Induced PARP and caspase-3 cleavage in SNU-620 and SNU-5 cells.

In Vivo

AMG 337 (0-30 mg/kg; p.o.; daily, for 28 d) inhibits MET signaling in tumor xenografts and inhibits tumor growth in MET-dependent tumor xenograft models[1].
AMG 337 (0-3 mg/kg; p.o.; once, for 3 or 24 h) is associated with increased necrosis in the MET-dependent SNU-620 tumor xenograft model[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female CD1 nu/nu mice bearing SNU-620, SNU-5, or U-87 MG xenografts[1]
Dosage:	0, 0.3, and 1 mg/kg (SNU-620 xenograft); 0, 0.3, 1, 3, and 10 mg/kg (SNU-5 xenograft); 0, 3, 10 and 30 mg/kg (U-87 xenograft)

Administration:	Oral administration; daily, for 28 days
Result:	Inhibited tumor growth in MET-dependent tumor xenograft models.

Animal Model:	Female CD1 nu/nu mice bearing SNU-620, SNU-5, or U-87 MG xenografts[1]
Dosage:	0.1, 0.5, 0.75, 1, 2, and 3 mg/kg
Administration:	Oral administration; once, for 3 hours
Result:	Inhibited Gab-1 phosphorylation in a dose-dependent manner.

Animal Model:	Female CD1 nu/nu mice with SNU-620 xenograft model (6-11 weeks of age; 20-26 g)[1]
Dosage:	0, 0.3, 1, and 3 mg/kg
Administration:	Oral administration; once, for 3 or 24 hours
Result:	Increased immunohistochemical staining with anti-caspase-3 antibody and decreased immunohistochemical staining with anti-BrdU antibody.

REFERENCES

[1]. Hughes PE, et, al. In Vitro and In Vivo Activity of AMG 337, a Potent and Selective MET Kinase Inhibitor, in MET-Dependent Cancer Models. Mol Cancer Ther. 2016 Jul;15(7):1568-79.

[2]. Du Z, et, al. Preclinical Evaluation of AMG 337, a Highly Selective Small Molecule MET Inhibitor, in Hepatocellular Carcinoma. Mol Cancer Ther. 2016 Jun;15(6):1227-37.

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