Capmatinib

Cat. No.: HY-13404

CAS No.: 1029712-80-8

Molecular Formula: $C_{23}H_{17}FN_6O$

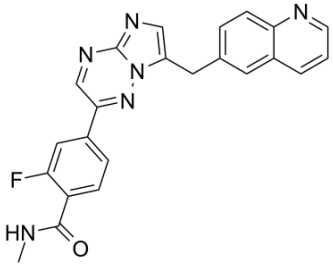
Molecular Weight: 412.42

Target: c-Met/HGFR; Apoptosis

Pathway: Protein Tyrosine Kinase/RTK; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (60.62 mM; Need ultrasonic)
H_2O : 10 mg/mL (24.25 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4247 mL	12.1236 mL	24.2471 mL
5 mM	0.4849 mL	2.4247 mL	4.8494 mL
10 mM	0.2425 mL	1.2124 mL	2.4247 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: ≥ 2.08 mg/mL (5.04 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.04 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Capmatinib (INC280; INCB28060) is a potent, orally active, selective, and ATP competitive c-Met kinase inhibitor (IC_{50}=0.13 nM). Capmatinib (INC280; INCB28060) potently inhibits c-MET-dependent tumor cell proliferation and migration and effectively induces apoptosis. Antitumor activity[1][2].

IC_{50} & Target

IC50: 0.13 nM (c-MET)[1]

In Vitro

Capmatinib (INCB28060) inhibits c-MET phosphorylation with an IC_{50} value of approximately 1 nM and a concentration of approximately 4 nM inhibits c-MET more than 90%. Capmatinib (INCB28060) inhibits SNU-5 viability or proliferation with an average IC_{50} value of 1.2 nM and a calculated IC_{90} value of 4.6 nM Capmatinib (INCB28060) prevents HGF-stimulated H441

	cell migration, with IC_{50} of approximately 2 nM. Again, there is little cell migration at a concentration of 16 nM Capmatinib (INCB28060). Capmatinib (INCB28060) potently and specifically inhibits c-MET enzyme activity, c-MET-mediated signal transduction, and the c-MET-dependent neoplastic phenotype of tumor cells. Capmatinib (INCB28060) exhibits strong antitumor activity in c-MET-dependent tumor models at well-tolerated doses. Capmatinib (INCB28060) exhibits picomolar enzymatic potency and is highly specific for c-MET with more than 10,000-fold selectivity over a large panel of human kinases. Capmatinib (INCB28060) potently inhibits c-MET-dependent tumor cell proliferation and migration and effectively induces apoptosis[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Oral dosing of Capmatinib (INCB28060) results in time- and dose-dependent inhibition of c-MET phosphorylation and tumor growth in c-MET-driven mouse tumor models, and the inhibitor is well tolerated at doses that achieve complete tumor inhibition. Furthermore, once daily dosing of 10 mg/kg Capmatinib (INCB28060) results in partial regressions in 6 of 10 U-87MG tumor-bearing mice. It is noted that in both S114 and U-87MG models, tumor growth inhibition increases with increased exposure of the compound and that tumor regressions could only be achieved when the compound exposure consistently exceeded 90% of c-MET inhibition. In these studies, Capmatinib (INCB28060) is well tolerated at all doses during the treatment periods, with no evidence of overt toxicity or weight loss[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Optimal cell density used in the viability assay is predetermined for individual cell lines. To determine compound potency, cells are seeded into 96-well microplates at the appropriate density in media containing 1% to 2% FBS and supplemented with serial dilutions of Capmatinib (INCB28060) in a final volume of 100 µL per well. After 72 hour incubation, 24 µL of CellTiter 96 AQueous One Solution is added to each well, and the plates are incubated for 2 hours in a 37°C incubator. The optical density is measured in the linear range using a microplate reader at 490 nm with wavelength correction at 650 nm. IC_{50} values are calculated using the GraphPad Prism Software[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Tumor-bearing mice are dosed orally, twice each day with 1, 3, 10, or 30 mg/kg of free base Capmatinib (INCB28060) reconstituted in 5% DMAC in 0.5% methylcellulose for up to 2 weeks. Body weights are monitored throughout the study as a gross measure of toxicity/morbidity. Tumor growth inhibition, expressed in percent, is calculated using the formula: (1−[(volume (treated)/volume (vehicle)])×100. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Cancer Res Treat. 2020 Jul;52(3):973-986.
- Biochem Biophys Rep. 2020 Jan 17;21:100726.
- Department Cancer Biology. Wayne State University. 2014 Jan.

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REFERENCES

[1]. Liu X, et al. A novel kinase inhibitor, INCB28060, blocks c-MET-dependent signaling, neoplastic activities, and cross-talk with EGFR and HER-3. Clin Cancer Res. 2011 Nov 15;17(22):7127-38.

[2]. Baltschukat S, et al. Capmatinib (INC280) Is Active Against Models of Non-Small Cell Lung Cancer and Other Cancer Types with Defined Mechanisms of MET Activation. Clin Cancer Res. 2019 May 15;25(10):3164-3175.

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