产品名称：**INCB28060**
产品别名：**Capmatinib**

生物活性：

Description	Capmatinib (INC280; INCB28060) is a potent, orally active, selective, and ATP competitive c-Met kinase inhibitor (IC50=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 IC50 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 IC50 value of 1.2 nM and a calculated IC90 value of 4.6 nM Capmatinib (INCB28060) prevents HGF-stimulated H441 cell migration, with IC50 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].
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].
Solvent&Solubility	***In Vitro:*** **DMSO : 12.66 mg/mL (30.70 mM;** Need ultrasonic and warming)

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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

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.

实验参考：

Cell Assay	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. IC50 values are calculated using the GraphPad Prism Software[1].
Animal Administration	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.
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.

源叶生物