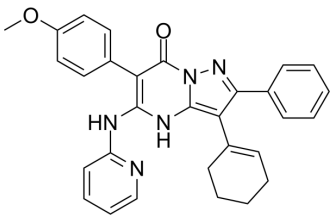
AG-270

Cat. No.:	HY-138630
CAS No.:	2201056-66-6
Molecular Formula:	$C_{30}H_{27}N_5O_2$
Molecular Weight:	489.57
Target:	Methionine Adenosyltransferase (MAT)
Pathway:	Epigenetics; Metabolic Enzyme/Protease
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 : 4 mg/mL (8.17 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0426 mL	10.2130 mL	20.4261 mL
	5 mM	0.4085 mL	2.0426 mL	4.0852 mL
	10 mM	---	---	---

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: ≥ 4.75 mg/mL (9.70 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 4.75 mg/mL (9.70 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AG-270 is an allosteric, noncompetitive, first-in-class, reversible and orally active MAT2A inhibitor, with an IC_{50} of 14 nM[1].

IC_{50} & Target

IC50: 14 nM (MAT2A)[1].

In Vitro

AG-270 demonstrates potent reduction in levels of intracellular SAM, as well as MTAP-null–selective antiproliferative activity in the HCT116 MTAP isogenic cell model in vitro[1].
AG-270 exhibits an IC_{50} of 20 nM in HCT116 MTAP-null cell SAM at 72 h[1].
MAT2A is a key enzyme in the methionine salvage pathway, responsible for generating the universal methyl donor, S-adenosylmethionine (SAM)[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

AG-270 shows excellent microsomal, hepatocyte, and in vivo metabolic stability across species (human, mouse, rat, dog, and monkey). AG-270 exhibits T1/2 values of 5.9 h, 4.2 h, 4.8 h and 21.3 h in mouse, rat, monkey and dog, respectively[1].
AG-270 (200 mg/kg, orally, q.d. for 38 days) results in dose-dependent reduction in tumor SAM levels and tumor growth of KP4 MTAP-null xenografts and is well tolerated, with mean body weight loss <5%[1].
Combining AG-270 with taxanes and gemcitabine yielded additive-tosynergistic antitumor activity, with the docetaxel combination yielding 50% complete tumor regressions in select models; combination benefits are observed in PDX models derived from esophageal, NSCLC, and pancreatic cancers[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Pancreatic KP4 MTAP-null xenograft mouse model[1].
Dosage:	10-200 mg/kg.
Administration:	Orally, q.d. for 38 days.
Result:	Led to dose-dependent reductions in tumor SAM levels and tumor growth of KP4 MTAP-null xenografts (TGI = 36% (10 mg/kg), 48% (30 mg/kg), 66% (100 mg/kg), 67% (200 mg/kg).

CUSTOMER VALIDATION

- FASEB J. 2022 Feb;36(2):e22167.

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REFERENCES

[1]. Zenon Konteatis, et al. Discovery of AG-270, a First-in-Class Oral MAT2A Inhibitor for the Treatment of Tumors with Homozygous MTAP Deletion. J Med Chem. 2021 Apr 8.

[2]. Marc L Hyer, et al. The MAT2A inhibitor AG-270 combines with both taxanes and gemcitabine to yield enhanced antitumor activity in patient-derived xenograft models.

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