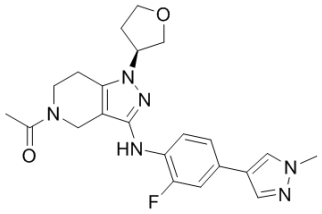
GNE-272

Cat. No.:	HY-100726
CAS No.:	1936428-93-1
Molecular Formula:	$C_{22}H_{25}FN_6O_2$
Molecular Weight:	424.47
Target:	Epigenetic Reader Domain; Histone Acetyltransferase
Pathway:	Epigenetics
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 : 100 mg/mL (235.59 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3559 mL	11.7794 mL	23.5588 mL
	5 mM	0.4712 mL	2.3559 mL	4.7118 mL
	10 mM	0.2356 mL	1.1779 mL	2.3559 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 (5.89 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.89 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.89 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GNE-272 is a potent and selective CBP/EP300 inhibitor with IC_{50} values of 0.02, 0.03 and 13 μM for CBP, EP300 and BRD4, respectively. GNE-272 is also a selective in vivo probe for CBP/EP300[1].

IC_{50} & Target

IC50: 0.02 μM (CBP), 0.03 μM (EP300), 13 μM (BRD4)[1]

In Vitro

GNE-272 is exquisitely selective for CBP/ EP300 and remarkably selective (650-fold) over BRD4. When tested at 10 μM in 35 kinase panel and 42 receptors off-target screening panel, GNE-272 does not inhibit any target at >30%. In addition, GNE-272

	does not inhibit (>10 μM, top concentration) several cytochrome P450s (3A4, 1A2, 2C9, 2C19, 2D6). The compound has good potency in the BRET cellular assay. In an orthogonal measure of the target engagement, GNE-272 is shown to inhibit the expression of MYC10 (MV4−11 cell line) with an EC_{50} of 0.91 μM and good correlation between the BRET and MYC cellular assays is observed[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	GNE-272 demonstrates low clearance following a 1 mg/ kg intravenous dose in a mouse PK experiment and good oral bioavailability when dosed at 100 mg/kg, reaching an unbound C_{max} of 26 μM. GNE-272 shows a marked antiproliferative effect in hematologic cancer cell lines and modulates MYC expression in vivo that corresponds with antitumor activity in an AML tumor model[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Human cancer cell lines (MOLM-16, HL-60, LP-1, KMS-34, Pfeiffer, DOHH-2) are treated for 4 h with 5 μM GNE-272 or DMSO control. After 6 days, cell viability is measured by CellTiter-Glo[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Mice are given 0 (vehicle, 0.5% methylcellulose; 0.2% Tween-80), 12.5, 25, and 50 mg/kg of GNE-272 by gavage, twice daily (BID) for 21 days in a volume of 100 μL. Tumor volumes are measured in two dimensions (length and width) using Ultra CalIV calipers and analyzed using Excel, version 11.2[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Crawford TD, et al. Discovery of a Potent and Selective in Vivo Probe (GNE-272) for the Bromodomains of CBP/EP300. J Med Chem. 2016 Dec 8;59(23):10549-10563.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA