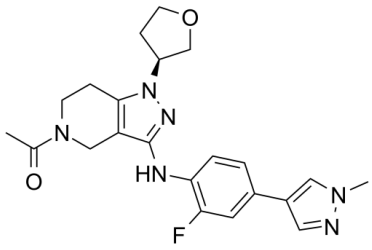
Data Sheet

Product Name:	GNE-272
Cat. No.:	CS-7493
CAS No.:	1936428-93-1
Molecular Formula:	C22H25FN6O2
Molecular Weight:	424.47
Target:	Epigenetic Reader Domain; Histone Acetyltransferase
Pathway:	Epigenetics
Solubility:	DMSO : 100 mg/mL (235.59 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

GNE-272 is a potent and selective in vivo probe for the bromodomains of **CBP/EP300** with **IC_{50}** values of 0.02, 0.03 and 13 μM for CBP, EP300 and BRD4, respectively. IC50 & 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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: GNE-272 is prepared in DMSO.[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]. **Animal Administration:** GNE-272 is prepared in 0.5% methylcellulose; 0.2% Tween-80.[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].

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.

CAIndexNames:

Ethanone, 1-[3-[[2-fluoro-4-(1-methyl-1H-pyrazol-4-yl)phenyl]amino]-1,4,6,7-tetrahydro-1-[(3S)-tetrahydro-3-furanyl]-5H-pyrazolo[4,3-c]pyridin-5-yl]-

SMILES:

CC(N1CCC2=C(C(NC3=C(F)C=C(C4=CN(C)N=C4)C=C3)=NN2[C@@H]5COCC5)C1)=O

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

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