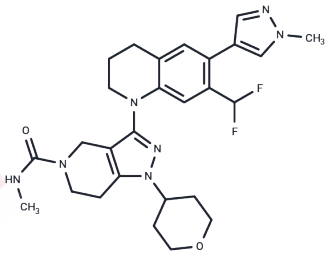
Data Sheet (Cat.No.T15405)

TargetMol

GNE-781

Chemical Properties



CAS No. : 1936422-33-1

Formula: C27H33F2N7O2

Molecular Weight: 525.59

Storage: Store at low temperature
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	GNE-781 is a highly potent and selective inhibitor of CBP (IC50: 0.94 nM in TR-FRET assay). GNE-781 also inhibits BRET and BRD4(1) (IC50s: 6.2 nM and 5100 nM, respectively).
Targets(IC50)	Epigenetic Reader Domain,Histone Acetyltransferase
In vitro	GNE-781 decreases FOXP3 (forkhead box P3) transcript levels. GNE-781 is a highly advanced potent and selective bromodomain inhibitor of cyclic adenosine monophosphate response element-binding protein, binding protein. GNE-781 is exquisitely selective for CBP/P300 and is remarkably selective for CBP (5425-fold) and P300 (4250-fold), which is shown by an examination of a subset of bromodomains. GNE-781 displays an appropriate balance of cell potency, selectivity (5425-fold over BRD4(1)) [1].
In vivo	GNE-781 is a highly potent and selective inhibitor of CBP that is efficacious in a MOLM-16 AML xenograft model. GNE-781 shows antitumor activity in an AML tumor model and is also shown to reduce Foxp3 transcript levels in a dose-dependent manner and it also shows moderate to low clearance in vivo in all species evaluated, with acceptable oral bioavailability. The effect of GNE-781 is determined in an in vivo PK/PD experiment using a MOLM-16 (adult AML cell line) xenograft mouse model. GNE-781(3 and 30 mg/kg; Single doses) are given in MOLM-16 tumor-bearing animals, and samples are collected at time points covering 2-24 h. Upon tumor establishment, Administration with GNE-781(3-30 mg/kg; twice daily). Single-agent efficacy is observed at all doses, as evidenced by inhibition of MOLM-16 tumor growth. Tumor growth inhibition (%TGI) is 73%, 71%, and 89% at 3, 10, and 30 mg/kg, respectively. All doses of GNE-781 are well tolerated over the 21-day dosing window, with a maximal body weight loss of 3.7%. Tumor RNA is generated and used to assess MYC transcript by quantitative RT-PCR relative to vehicle-treated animals. At doses as low as 3 mg/kg at 2 and 8 h, suppression of MYC is observed, with maximal suppression observed at 10 and 30 mg/kg at 2 h (87% and 88% inhibition, respectively). To evaluate the in vivo efficacy of GNE-781, MOLM-16 AML xenografts are established in SCID beige mice[1].

Solubility Information

Solubility	DMSO: 95 mg/mL (180.75 mM),Sonication is recommended. Ethanol: 95 mg/mL (180.75 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (3.81 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.9026 mL	9.5131 mL	19.0262 mL
5 mM	0.3805 mL	1.9026 mL	3.8052 mL
10 mM	0.1903 mL	0.9513 mL	1.9026 mL
50 mM	0.0381 mL	0.1903 mL	0.3805 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Romero FA, et al. GNE-781, A Highly Advanced Potent and Selective Bromodomain Inhibitor of Cyclic Adenosine Monophosphate Response Element Binding Protein, Binding Protein (CBP). J Med Chem. 2017 Nov 22;60(22):9162-9183.

Wang L, Wu J, Sramek M, et al.Heterogeneous enhancer states orchestrate β cell responses to metabolic stress. Nature Communications.2024, 15(1): 9361.