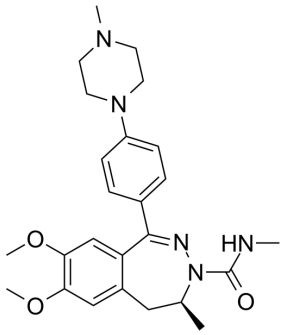
BAY1238097

Cat. No.:	HY-112316
CAS No.:	1564268-08-1
Molecular Formula:	$C_{25}H_{33}N_5O_3$
Molecular Weight:	451.56
Target:	Epigenetic Reader Domain
Pathway:	Epigenetics
Storage:	4°C, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 150 mg/mL (332.18 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2145 mL	11.0727 mL	22.1455 mL
5 mM	0.4429 mL	2.2145 mL	4.4291 mL
10 mM	0.2215 mL	1.1073 mL	2.2145 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 (5.54 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.54 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.54 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BAY1238097 is a potent and selective inhibitor of BET binding to histones and has strong anti-proliferative activity in different AML (acute myeloid leukemia) and MM (multiple myeloma) models through down-regulation of c-Myc levels and its downstream transcriptome (IC_{50} <100 nM).

IC_{50} & Target

IC50: < 100 nM (BET in a TR-FRET assay)[1].

In Vitro

BAY 1238097 shows strong inhibitory activity (IC_{50} < 100 nM) in a TR-FRET assay using BET BRD4 bromodomain 1 and an acetylated peptide derived from histone H4. In the NanoBRET assay, the interaction between BRD4 (IC_{50}=63 nM), BRD3 or BRD2 (IC_{50}=609 nM) and H4 (IC_{50}=2430 nM) is inhibited[1].

BAY 1238097 has in vitro anti-tumour activity in lymphoma models. BAY 1238097 affects the gene expression of GCB DLBCL cells. At the gene level, BTK, CCDC86, CCND2, CD19, CD27, FAIM, FCMR (FAIM3), IL7R, IRAK1, MAPK13, MYB, MYC, PDE4B, TNFRSF13B, TNFRSF17 are among the top downregulated genes. Beside histone-coding genes, the upregulated genes include CCL5, CDKN2C, CD69, JUN, and MKNK2[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

BAY 1238097 shows strong efficacy in the AML and MM models. BAY 1238097 has in vivo anti-tumour activity in lymphoma models[1][2].

BAY 1238097 is well tolerated at 10-15 mg/kg applied daily over 9-14 days in different disease models, with no obvious toxicity[1][2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Severe combined immunodeficiency (SCID) female mice (9-12 weeks old) inoculated subcutaneously into the right flank with 5×10^6 SU-DHL-8 cells/mouse suspended in 0.1 mL of matrigel or with O
Dosage:	15 mg/kg (maximal tolerated dose).
Administration:	Orally daily for 12 days (on day 21 post-tumour inoculation).
Result:	Showed strong efficacy in the AML models THP-1, MOLM-13 and KG-1, with T/C between 13 and 20%. Also active in MM models in a human IGH-cyclin D1 translocated MOLP-8 model with a T/C of 3%[2].

REFERENCES

[1]. Lejeune, P., et al. (2015) Abstract 3524: BAY 1238097, a novel BET inhibitor with strong efficacy in hematological tumor models. Cancer Research, 75(15 Suppl), 884.

[2]. Bernasconi E, et al. Preclinical evaluation of the BET bromodomain inhibitor BAY 1238097 for the treatment of lymphoma. Br J Haematol. 2017 Sep;178(6):936-948.

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