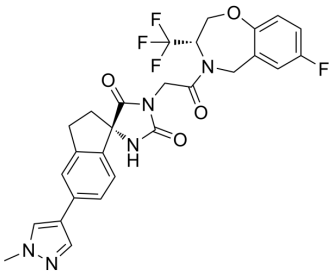
B026

Cat. No.:	HY-147261
CAS No.:	2379416-48-3
Molecular Formula:	$C_{27}H_{23}F_4N_5O_4$
Molecular Weight:	557.5
Target:	Histone Acetyltransferase
Pathway:	Epigenetics
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

B026 is a selective, potent, orally active p300/CBP histone acetyltransferase (HAT) inhibitor with IC_{50} values of 1.8 nM and 9.5 nM for p300 and CBP enzyme, respectively. B026 has anticancer activity for androgen receptor-positive (AR+) prostate cancer cell lines[1].

IC_{50} & Target

p300	CBP
8.1 nM (IC_{50})	9.5 nM (IC_{50})

In Vitro

B026 (0-5 μM; 12 h; cancer cell lines) has antiproliferative activity[1].
B026 (0-5 μM; 6 h; MV-4-11 cells) exhibits inhibitory effects on H3K27Ac expression[1].
B026 (0-5 μM; 12 h; MV-4-11 cells) targets the cellular p300 protein and increases the thermal stability of p300 protein in a dose-dependent manner[1].
B026 (0-1 μM; 24 h; MV-4-11 cells) decreases the expression of MYC, which a key oncogenictranscription factor that is regulated by superenhancer regions containing p300/CBP[1].

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

Cell Viability Assay[1]

Cell Line:	Maver-1, MV-4-11, K562, Kasumi-1, LnCaP-FGC and 22Rv1 cells
Concentration:	0-5 μM
Incubation Time:	12 hours
Result:	Inhibited cell growth with IC_{50} values of 2.6, 4.2, 4.4, 9.8, 40.5 and 104.4 nM for Maver-1, MV-4-11, 22Rv1, LnCaP-FGC, Kasumi-1 and K562 cells, respectively.

Western Blot Analysis[1]

Cell Line:	MV-4-11 cells
Concentration:	0, 0.313, 0.625, 1.25, 2.5 and 5 μM
Incubation Time:	6 hours
Result:	Decreased the expression of H3K27Ac in a dose-dependent manner.

In Vivo

B026 (1-3 mg/kg; i.v. and p.o.; 0-24 h; male SD rats) has a low clearance (13.4 mL/min/kg) and good oral exposure (AUC=3.71 μM·h) with good oral bioavailability (F=56%) in rat[1].

B026 (50-100 mg/kg; p.o.; daily, for 28 days; balb/c female mice) inhibits tumor growth in a dose-dependent manner[1].

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Animal Model:	Balb/c female mice with MV-4-11 xenograft[1]
Dosage:	50 and 100 mg/kg
Administration:	Oral administration; daily, for 28 days
Result:	Inhibited tumor growth with TGI of 75.0% at 50 mg/kg and 85.7% at 100 mg/kg, respectively.

Animal Model:	Male SD rats[1]
Dosage:	1 and 3 mg/kg
Administration:	Intravenous injection and oral administration; 0.25, 0.5 , 1 , 2 , 4 , 8 and 24 hours

Result:

Administration	i.v. (1 mg/kg)	p.o. (3 mg/kg)
$T_{1/2}$ (h)	1.5	1.02
T_{max} (h)		0.83
C_{max} (μM)		1.12
AUC_{last} (μM·h)	2.22	3.71
Vd_{ss} (L/kg)	1.5	
$CL_{\_obs}$ (mL/min/kg)	13.4	
PPB %		98.2
F %		56

REFERENCES

[1]. Yang Y, et, al. Discovery of Highly Potent, Selective, and Orally Efficacious p300/CBP Histone Acetyltransferases Inhibitors. J Med Chem. 2020 Feb 13;63(3):1337-1360.

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

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