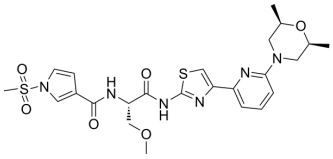
FHD-286

Cat. No.:	HY-144835
CAS No.:	2671128-05-3
Molecular Formula:	$C_{24}H_{30}N_6O_6S_2$
Molecular Weight:	562.66
Target:	Epigenetic Reader Domain; Oxidative Phosphorylation
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 : 250 mg/mL (444.32 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7773 mL	8.8864 mL	17.7727 mL
	5 mM	0.3555 mL	1.7773 mL	3.5545 mL
	10 mM	0.1777 mL	0.8886 mL	1.7773 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.70 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.70 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

FHD-286 is a selective, oral inhibitor of SMARCA4/SMARCA2 ATPase (BRG1 and BRM) inhibitor. FHD-286 has the potential for the research of BAF (BRG1/BRM-associated factor)-related disorders such as acute myeloid leukemia[1].

In Vitro

FHD-286 (10 to 100 nM) for 7 days induces differentiation followed by loss of viability of AML cell lines and PD AML cells with MLL rearrangement (r), mutant (mt) NPM1 and chromosome 3q26 lesions (with EVI1 overexpression). Treatment with FHD-286 causes whole-genome, concordant, up- or down-regulations in ATAC-Seq peaks and RNA-Seq-determined mRNA expressions of specific loci, associated with significant reduction in the gene-sets of targets of MYC, mTORC1, E2F, Interferon-gamma, IL6-JAK-STAT3, as well as of inflammatory response and oxidative phosphorylation genes. QPCR analyses determined significant reduction in mRNA expression of MYC, SPI1 and BCL2 genes. Mass spectrometry on AML cell lysates treated with FHD-286 showed log2 fold-reductions in c-Myc, SPI1, MEF2C, KMT2C and CDK4 (in MOLM13) and in EVI1,

	c-Myb, CDK6 and c-Myc (in AML191) cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	FHD-286 (1.5 mg/kg; oral administration; for 10 days) increases in IFNγ and Th1-type chemokine CXCL10 levels[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	B16F10 tumor-bearing mice[2]
Dosage:	1.5 mg/kg
Administration:	Oral administration; for 10 days
Result:	Increased in IFNγ and Th1-type chemokine CXCL10 levels.

REFERENCES

[1]. Kana Ichikawa, et al. Synergistic efficacy of the BRM/BRG1 ATPase inhibitor, FHD-286, and anti-PD-1 antibody in mouse syngeneic tumor models.

[2]. Warren C. Fiskus, et al. Abstract 1140: Pre-clinical efficacy of targeting BAF complexes through inhibition of the dual ATPases BRG1 and BRM by FHD-286 in cellular models of AML. Cancer Res (2023) 83 (7_Supplement): 1140.

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