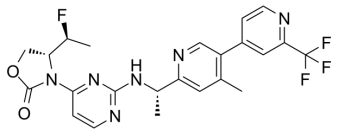
IDH-305

Cat. No.:	HY-104036
CAS No.:	1628805-46-8
Molecular Formula:	$C_{23}H_{22}F_4N_6O_2$
Molecular Weight:	490.45
Target:	Isocitrate Dehydrogenase (IDH)
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 150 mg/mL (305.84 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0389 mL	10.1947 mL	20.3894 mL
5 mM	0.4078 mL	2.0389 mL	4.0779 mL
10 mM	0.2039 mL	1.0195 mL	2.0389 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 (5.10 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.10 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

IDH-305 is an orally available, mutant-selective and brain-penetrant IDH1 inhibitor that targets IDH1 (R132) mutation. IDH-305 exhibits greater than 200 fold selectivity for mutant IDH1 isoforms vs. WT (IC_{50}= 27 nM ($IDH1^{R132H}$), 28 nM ($IDH1^{R132C}$), 6.14 μM ($IDH1^{WT}$))[1][2].

IC_{50} & Target

IC50: 27 nM ($IDH1^{R132H}$), 28 nM ($IDH1^{R132C}$), 6.14 μM ($IDH1^{WT}$)[1]

In Vitro

IDH-305 inhibits HCT116-$IDH1^{R132H+/-}$ cells with an IC_{50} of 24 nM[1].

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

In Vivo

IDH-305 (30-300 mg/kg; p.o.; twice daily for 21 days) inhibits 2-HG production and 2-HG-dependent tumor growth of an IDH1 mutant PDX melanoma model[1].

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

Animal Model:	nu/nu mice (HMEX2838-IDH1$^{R132C+/-}$PDX model)[1]
Dosage:	30, 100, 300 mg/kg
Administration:	Oral gavage; twice daily for 21 days
Result:	Resulted in 62-67% 2-HG reduction and significant anti-tumor activity at 100 mg/kg and 97-99% 2-HG reduction and partial tumor regression of 32% at 300 mg/kg.

REFERENCES

[1]. Cho YS, et al. Discovery and Evaluation of Clinical Candidate IDH305, a Brain Penetrant Mutant IDH1 Inhibitor. ACS Med Chem Lett. 2017 Sep 18;8(10):1116-1121.

[2]. Courtney D DiNardo, et al. A Phase I Study of IDH305 in Patients with Advanced Malignancies Including Relapsed/Refractory AML and MDS That Harbor IDH1R132 Mutations. Blood, 128(22), 1073.

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