Tovinontrine

Cat. No.: HY-109193

CAS No.: 2062661-53-2

Molecular Formula: $C_{21}H_{26}N_6O_2$

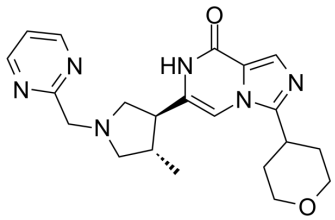
Molecular Weight: 394.47

Target: Phosphodiesterase (PDE)

Pathway: Metabolic Enzyme/Protease

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 : 100 mg/mL (253.50 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5350 mL	12.6752 mL	25.3505 mL
	5 mM	0.5070 mL	2.5350 mL	5.0701 mL
	10 mM	0.2535 mL	1.2675 mL	2.5350 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 (6.34 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.34 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.34 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tovinontrine (IMR-687) is a highly potent and selective phosphodiesterase-9 (PDE9) inhibitor specifically for the treatment of sickle cell disease. IC_{50}s are 8.19 nM and 9.99 nM for PDE9A1 and PDE9A2, respectively[1].

IC_{50} & Target

PDE9A1 8.19 nM	PDE9A2 9.99 nM	PDE1A3 88.4 nM	PDE1B 8.48 nM
PDE1C 12.2 nM	PDE5A2 81.9 nM		

In Vitro	IMR-687 inhibits PDE9A with more than 800-fold greater potency than PDE1A3, PDE1B, PDE1C, PDE5A2, with IC_{50} values of 88.4 μM, 8.48 μM, 12.2 μM, and 81.9 μM, respectively[1]. IMR-687 (0.1-10 μM) treatment in erythroid K562 cells for 72 hours induces hemoglobin (HbF) in a dose-dependent manner[1]. IMR-687 (0.03-10 μM) treatment for 6 hours in erythroid K562 cells increases cGMP in a dose-dependent manner[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	IMR-687 (30 mg/kg/day; after 30 days of treatment) shows a greater than 3-fold in the percent of HbF^+ F-cells (8.4% in vehicle treated and 27.3% in IMR-687 treated) and a corresponding 2-fold decrease in sickled red blood cells (56.3% in vehicle treated and 24.4% in IMR-687 treated)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	HbSS-Townes mice on a 129/B6 background (10-12 weeks old) [1]
Dosage:	30 mg/kg
Administration:	Dosed daily by gavage for 30 days
Result:	Resulted in fetal hemoglobin (HbF) induction, reduced hemolysis and reduced reticulocytosis.

REFERENCES

[1]. James G McArthur, et al. A novel, highly potent and selective phosphodiesterase-9 inhibitor for the treatment of sickle cell disease. Haematologica. 2020 Mar;105(3):623-631.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA