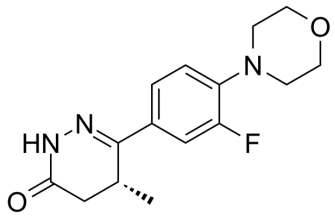
BRD9500

Cat. No.:	HY-136350
CAS No.:	1630760-75-6
Molecular Formula:	$C_{15}H_{18}FN_3O_2$
Molecular Weight:	291.32
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 : 50 mg/mL (171.63 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.4327 mL	17.1633 mL	34.3265 mL
	5 mM	0.6865 mL	3.4327 mL	6.8653 mL
	10 mM	0.3433 mL	1.7163 mL	3.4327 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 (8.58 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (8.58 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.58 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BRD9500 is an orally active phosphodiesterases 3 (PDE3) inhibitor with IC_{50}s of 10 and 27 nM for PDE3A and PDE3B, respectively. Antitumor activity[1].

IC_{50} & Target

PDE3A	PDE3B
10 nM (IC_{50})	27 nM (IC_{50})

In Vitro

BRD9500 is a DNMDP analog. DNMDP potently and selectively inhibits PDE3A and PDE3B and kills cancer cells by inducing

PDE3A/B interactions with SFLN12[1].
BRD9500 exhibits an EC_{50} of 1 nM for SK-MEL-3 melanoma cell line viability[1].
BRD9500 exhibits an EC_{50} of 1.6 nM for HeLa viability[1].
BRD9500 (10 μM; 8 hours) stabilizes the PDE3A-SLFN12 interaction in HeLa cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	HeLa cells
Concentration:	10 μM
Incubation Time:	8 hours
Result:	SLFN12 coimmunoprecipitation was analyzed by immunoblotting with an anti-V5 antibody to detect the SLFN12-V5 fusion protein. The SLFN12-V5 was clearly detected with the anti-V5 antibody.

In Vivo

BRD9500 (10, 20, and 50 mg/kg; orally) inhibits SK-MEL-3 melanoma growth in mice[1].
BRD9500 shows high plasma levels in mice after iv (1 mg/kg) as well as po (2 mg/kg) dosing over eight hours making it a valuable candidate for in vivo xenograft testing[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female NMRI nude mice bearing SK-MEL-3 melanoma cells tumor xenografts[1]
Dosage:	10, 20, and 50 mg/kg
Administration:	Orally at 10 and 20 mg/kg twice daily (2QD) and at 50 mg/kg once per day (QD).
Result:	Achieved the strongest antitumor activity at 50 mg/kg. All treatments were well tolerated without critical body weight loss or toxicities.

REFERENCES

[1]. Timothy A Lewis, et al. Optimization of PDE3A Modulators for SLFN12-Dependent Cancer Cell Killing. ACS Med Chem Lett. 2019 Oct 18;10(11):1537-1542.

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