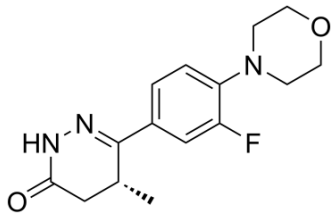
BRD9500

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



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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