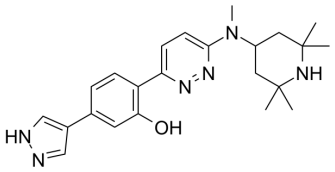
NVS-SM2

Cat. No.:	HY-111520
CAS No.:	1562333-92-9
Molecular Formula:	$C_{23}H_{30}N_6O$
Molecular Weight:	406.52
Target:	DNA/RNA Synthesis
Pathway:	Cell Cycle/DNA Damage
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 75 mg/mL (184.49 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4599 mL	12.2995 mL	24.5990 mL
5 mM	0.4920 mL	2.4599 mL	4.9198 mL
10 mM	0.2460 mL	1.2300 mL	2.4599 mL

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

BIOLOGICAL ACTIVITY

Description

NVS-SM2 is a potent, orally active and brain-penetrant SMN2 splicing enhancer with an EC_{50} of 2 nM for SMN. NVS-SM2 enhances U1-pre-mRNA association. NVS-SM2 promotes exon 7 inclusion and restores normal survival motor neuron (SMN) protein expression. NVS-SM2 can be used for spinal muscular atrophy (SMA) research[1][2].

IC_{50} & Target

EC50: 5 nM (SMN)[1]

In Vitro

For NVS-SM2, the molecular mechanism of action is via stabilization of the transient double-strand RNA structure formed by the SMN2 pre-mRNA and U1 small nuclear ribonucleic protein (snRNP) complex. The binding affinity of U1 snRNP to the 5' splice site is increased in a sequence-selective manner, discrete from constitutive recognition[1].

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

In Vivo

NVS-SM2 (0.1-1 mg/kg; s.c.; for 30 days) treatment extends survival in a severe SMA mouse model[2].

Pharmacokinetic analysis demonstrate that NVS-SM2 is readily available in the brain after IV and oral (PO) administration in mouse and rat with T_{max} of 3 h after PO with 3 mg/kg in mice, and NVS-SM2 treatment induces a 1.5-fold increase in SMN protein levels in the mouse brain[1].

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

Animal Model:	Severe SMA mice[2]
Dosage:	0.1 mg/kg and 1 mg/kg
Administration:	Subcutaneous injection; daily from day 2 to day 15, followed by every other day until day 30
Result:	Extended survival in a severe SMA mouse model.

REFERENCES

[1]. James Palacino, et al. SMN2 splice modulators enhance U1-pre-mRNA association and rescue SMA mice. Nat Chem Biol. 2015 Jul;11(7):511-7.

[2]. Anne Rietz, et al. Short-duration splice promoting compound enables a tunable mouse model of spinal muscular atrophy. Life Sci Alliance. 2020 Nov 24;4(1):e202000889.

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