Branaplam

Cat. No.: HY-19620

CAS No.: 1562338-42-4

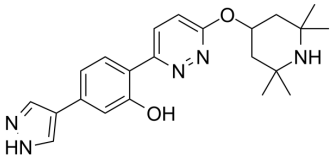
Molecular Formula: $C_{22}H_{27}N_5O_2$

Molecular Weight: 393.48

Target: DNA/RNA Synthesis; Potassium Channel

Pathway: Cell Cycle/DNA Damage; Membrane Transporter/Ion Channel

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 6.12 mg/mL (15.55 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5414 mL	12.7071 mL	25.4143 mL
	5 mM	0.5083 mL	2.5414 mL	5.0829 mL
	10 mM	0.2541 mL	1.2707 mL	2.5414 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: ≥ 1 mg/mL (2.54 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.71 mg/mL (1.80 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 0.71 mg/mL (1.80 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 0.57 mg/mL (1.45 mM); Clear solution
5. Add each solvent one by one: 1% DMSO >> 99% saline
   Solubility: 0.12 mg/mL (0.30 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Branaplam (LMI070; NVS-SM1) is a highly potent, selective and orally active survival motor neuron-2 (SMN2) splicing modulator with an EC_{50} of 20 nM for SMN. Branaplam inhibits human-ether-a-go-go-related gene (hERG) with an IC_{50} of 6.3 μM. Branaplam elevates full-length SMN protein and extends survival in a severe spinal muscular atrophy (SMA) mouse model [1][2].

IC_{50} & Target	IC50: 20 nM (SMN)[1] EC50: 6.3 μM (hERG)[2]
In Vitro	Branaplam (LMI070; NVS-SM1) treatment induces changes in the levels of 175 genes in human fibroblasts[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Branaplam (LMI070; NVS-SM1; 3, 10, 30 mg/kg; oral) produces dose-dependent elevations of SMN2-FL transcript and SMN protein in brain and spinal cord[1]. Branaplam (1 mg/kg of IV; 3 mg/kg of PO) has a CL of 25 mL/min/kg and an AUC of 3.03 μM•h[2]. A single Branaplam (oral; 30 mg/kg) results in significant and durable SMN protein elevation in brain for up to 160 hours in C/+ mice[1]. Branaplam (oral; 0.03, 0.1, 0.3, 1, 3 mg/kg) improves body weight and extendes lifespan in n SMNΔ7 mice[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	C/+ SMA mouse model[1]
Dosage:	3, 10, 30 mg/kg
Administration:	Oral
Result:	Produced dose-dependent elevations of SMN2-FL transcript and SMN protein in brain and spinal cord.

Animal Model:	Male Sprague-Dawley rat[2]
Dosage:	1 mg/kg (IV);3 mg/kg (PO) (Pharmacokinetic Analysis)
Administration:	IV or PO
Result:	Had a CL of 25 mL/min/kg and an AUC of 3.03 μM•h.

CUSTOMER VALIDATION

- Nucleic Acids Res. 2021 Aug 6;gkab650.
- bioRxiv. 2020 Jun.
- bioRxiv. 2020 Feb.

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REFERENCES

[1]. Palacino J, et al. SMN2 splice modulators enhance U1-pre-mRNA association and rescue SMA mice. Nat Chem Biol. 2015 Jul;11(7):511-517.

[2]. Cheung AK, et al. Discovery of Small Molecule Splicing Modulators of Survival Motor Neuron-2 (SMN2) for the Treatment of Spinal Muscular Atrophy (SMA). J Med Chem. 2018 Dec 27;61(24):11021-11036.

Caution: Product has not been fully validated for medical applications. For research use only.

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