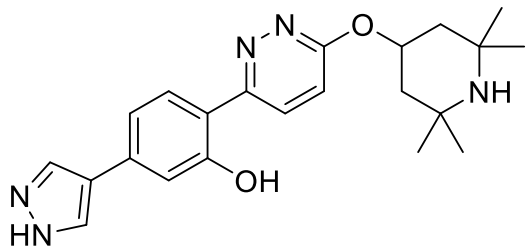
Product data sheet

MedKoo Cat#: 526827 Name: Branaplam free base CAS#: 1562338-42-4 (free base) Chemical Formula: $C_{22}H_{27}N_5O_2$ Exact Mass: 393.2165 Molecular Weight: 393.491	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Branaplam, also known as NVS-SM1 and LMI-070, is a highly potent, selective and orally active small molecule SMN2 splicing modulator as a potential treatment for SMA Type 1 (Spinal Muscular Atrophy) .NVS-SM1 works by increasing the amount of functional SMN protein produced by the "back-up" gene, SMN2, through modifying its splicing.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	3	7.62

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.54 mL	12.71 mL	25.41 mL
5 mM	0.51 mL	2.54 mL	5.08 mL
10 mM	0.25 mL	1.27 mL	2.54 mL
50 mM	0.05 mL	0.25 mL	0.51 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Palacino J, Swalley SE, Song C, Cheung AK, Shu L, Zhang X, Van Hoosear M, Shin Y, Chin DN, Keller CG, Beibel M, Renaud NA, Smith TM, Salcius M, Shi X, Hild M, Servais R, Jain M, Deng L, Bullock C, McLellan M, Schuierer S, Murphy L, Blommers MJ, Blaustein C, Berenshteyn F, Lacoste A, Thomas JR, Roma G, Michaud GA, Tseng BS, Porter JA, Myer VE, Tallarico JA, Hamann LG, Curtis D, Fishman MC, Dietrich WF, Dales NA, Sivasankaran R. SMN2 splice modulators enhance U1-pre-mRNA association and rescue SMA mice. Nat Chem Biol. 2015 Jul;11(7):511-7. doi: 10.1038/nchembio.1837. Epub 2015 Jun 1. Erratum in: Nat Chem Biol. 2015 Sep;11(9):741. Erratum in: Nat Chem Biol. 2016 Apr;12(4):304. PMID: 26030728.

In vivo study

1. Palacino J, Swalley SE, Song C, Cheung AK, Shu L, Zhang X, Van Hoosear M, Shin Y, Chin DN, Keller CG, Beibel M, Renaud NA, Smith TM, Salcius M, Shi X, Hild M, Servais R, Jain M, Deng L, Bullock C, McLellan M, Schuierer S, Murphy L, Blommers MJ, Blaustein C, Berenshteyn F, Lacoste A, Thomas JR, Roma G, Michaud GA, Tseng BS, Porter JA, Myer VE, Tallarico JA, Hamann LG, Curtis D, Fishman MC, Dietrich WF, Dales NA, Sivasankaran R. SMN2 splice modulators enhance U1-pre-mRNA association and rescue SMA mice. Nat Chem Biol. 2015 Jul;11(7):511-7. doi: 10.1038/nchembio.1837. Epub 2015 Jun 1. Erratum in: Nat Chem Biol. 2015 Sep;11(9):741. Erratum in: Nat Chem Biol. 2016 Apr;12(4):304. PMID: 26030728.

Product data sheet

2. Cheung AK, Hurley B, Kerrigan R, Shu L, Chin DN, Shen Y, O'Brien G, Sung MJ, Hou Y, Axford J, Cody E, Sun R, Fazal A, Fridrich C, Sanchez CC, Tomlinson RC, Jain M, Deng L, Hoffmaster K, Song C, Van Hoosear M, Shin Y, Servais R, Towler C, Hild M, Curtis D, Dietrich WF, Hamann LG, Briner K, Chen KS, Kobayashi D, Sivasankaran R, Dales NA. 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. doi: 10.1021/acs.jmedchem.8b01291. Epub 2018 Dec 13. PMID: 30407821.

7. Bioactivity

Biological target:

Branaplam (LMI070) is a highly selective, small-molecule splicing modulators of survival motor neuron-2 (SMN2) with an EC50 of 0.02 μM.

In vitro activity

In the cellular setting, it was observed that SMN protein levels remained elevated after compound treatment, which and suggests that SMN protein has a long half-life. Branaplam (LMI070; NVS-SM1) treatment induces changes in the levels of 175 genes in human fibroblasts.

Reference: Nat Chem Biol. 2015 Jul;11(7):511-7. https://doi.org/10.1038/nchembio.1837

In vivo activity

The C/+ SMA mouse model was employed. After oral administration, NVS-SM1 produced dose-dependent elevations of SMN2-FL transcript and SMN protein in brain and spinal cord (Fig. 2a,b), thus establishing translatability and a pharmacokinetic-pharmacodynamic relationship. Although it showed dose-responsive activity in the C/+ model (Fig. 2a,b), NVS-SM1 exhibited efficacy at lower doses and exposures. NVS-SM1 showed robust activity across disease-relevant induced pluripotent stem cell (iPSc)-derived neurons (Supplementary Fig. 2a,b). It was also demonstrated that the desired transcript response in SMA-type III PBMCs after NVS-SM1 treatment, suggesting that this readout could serve as a peripheral pharmacodynamic marker in the clinic (Supplementary Fig. 2c). A single, 30 mg per kg body weight oral dose of NVS-SM1 resulted in significant ($P < 0.05$) and durable SMN protein elevation in brain for up to 160 h (Fig. 2c).

Reference: Nat Chem Biol. 2015 Jul;11(7):511-7. https://doi.org/10.1038/nchembio.1837

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.