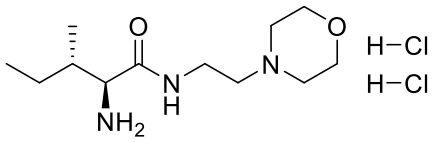
Product data sheet

MedKoo Cat#: 555874 Name: LM11A-31 HCl CAS#: 1243259-19-9 (HCl) Chemical Formula: $C_{12}H_{27}Cl_2N_3O_2$ Molecular Weight: 316.267	
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:

LM11A-31 is a small-molecule p75NTR modulator and proNGF antagonist, in preventing diabetes-induced BRB breakdown. Targeting p75NTR signalling using LM11A-31, an orally bioavailable receptor modulator, may offer an effective, safe and non-invasive therapeutic strategy for treating macular oedema, a major cause of blindness in diabetes.

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	40.8	129.05
H2O	78.0	247.62

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.16 mL	15.81 mL	31.62 mL
5 mM	0.63 mL	3.16 mL	6.32 mL
10 mM	0.32 mL	1.58 mL	3.16 mL
50 mM	0.06 mL	0.32 mL	0.63 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. Meeker RB, Poulton W, Feng WH, Hudson L, Longo FM. Suppression of immunodeficiency virus-associated neural damage by the p75 neurotrophin receptor ligand, LM11A-31, in an in vitro feline model. J Neuroimmune Pharmacol. 2012 Jun;7(2):388-400. doi: 10.1007/s11481-011-9325-0. Epub 2011 Dec 10. PMID: 22161560; PMCID: PMC3746485.
2. Yang T, Tran KC, Zeng AY, Massa SM, Longo FM. Small molecule modulation of the p75 neurotrophin receptor inhibits multiple amyloid beta-induced tau pathologies. Sci Rep. 2020 Nov 23;10(1):20322. doi: 10.1038/s41598-020-77210-y. PMID: 33230162; PMCID: PMC7683564.

In vivo study

1. Yin GN, Ock J, Limanjaya A, Minh NN, Hong SS, Yang T, Longo FM, Ryu JK, Suh JK. Oral Administration of the p75 Neurotrophin Receptor Modulator, LM11A-31, Improves Erectile Function in a Mouse Model of Cavernous Nerve Injury. J Sex Med. 2021 Jan;18(1):17-28. doi: 10.1016/j.jsxm.2020.10.015. Epub 2020 Nov 24. PMID: 33243690.
2. Simmons DA, Knowles JK, Belichenko NP, Banerjee G, Finkle C, Massa SM, Longo FM. A small molecule p75NTR ligand, LM11A-31, reverses cholinergic neurite dystrophy in Alzheimer's disease mouse models with mid- to late-stage disease progression. PLoS One. 2014 Aug 25;9(8):e102136. doi: 10.1371/journal.pone.0102136. PMID: 25153701; PMCID: PMC4143160.

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7. Bioactivity

Biological target:

LM11A-31 dihydrochloride, a non-peptide p75NTR (neurotrophin receptor p75) modulator, is a potent proNGF (nerve growth factor) antagonist.

In vitro activity

To test the effects of LM11A-31 in the presence of FIV (feline immunodeficiency virus), feline neural cultures at 12 days in culture were inoculated with 105 TCID50 FIV mix followed immediately by addition of LM11A-31 at a concentration of 10 nM. LM11A-31 was sustained in the culture throughout the experiment and the cells were fixed at 3 and 7 days post-treatment and stained for MAP-2 and GFAP. The FIV inoculated cultures showed damage after seven days which is illustrated in Figure 3A. Beading and simplification of MAP-2+ processes and neuron shrinkage was seen as in Figure 1 and a co-stain for GFAP stain also showed a retraction of astrocyte processes with development of a more process bearing morphology. Treatment with LM11A-31 reversed much of this damage with most cultures showing healthy neurons with elaborate processes on a more uniform bed of astrocytes (Figure 3B). Quantification of the MAP-2 stain shown in Figure 4, illustrates the mean (± sem) MAP-2 fluorescence intensity relative to untreated control cultures at three days and seven days post-inoculation. At three days no decrease in MAP-2 stain or changes in neuron morphology were seen (94.8 ± 7.1% of control) and by seven days a 58% decrease was seen (41.8 ± 15.7% of control, p=0.0049). In each case, treatment with LM11A-31 resulted in MAP-2 staining that was above the control values (172–193%) and 4-fold greater than the MAP-2 intensity of the neural cultures treated with FIV (FIV+LM11A-31 vs. FIV at 7 days, p=0.0111). The strong neuroprotection afforded by LM11A-31 in an infectious in vitro model indicates that LM11A-31 may have excellent potential for the treatment of HIV-associated neurodegeneration.

Rerference: J Neuroimmune Pharmacol. 2012 Jun; 7(2): 388–400. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3746485/

In vivo activity

To further assess the robustness of the effect of LM11A-31 in slowing progression of degeneration due to Alzheimer's disease (AD), it was determined whether the ligand would be effective in reducing neurite degeneration in another well-characterized AD mouse model, Tg2576 mice. LM11A-31 was administered to female Tg2576 mice and their nTg littermates for 3 months starting at 14 months of age. In these mice, cognitive deficits are seen at 3 months of age and are progressive. Insoluble Aβ levels incrementally increase beginning at 6 months of age and Aβ deposition is evident at 11 months. Cholinergic dystrophic neurites are not seen at 8 months of age but occur in the cortex by 16 months. In comparison to nTg mice, vehicle-treated Tg2576 mice at 17 months old had shorter ChAT-stained neurites in the basal forebrain that occupied less area (Fig. 10A,B). These deficits were prevented in Tg2576 mice given LM11A-31, which had cholinergic neurites resembling those of nTg mice. Dendrite branching complexity was also decreased in vehicle-treated Tg2576 mice but not in those given LM11A-31, compared to nTg mice (Fig. 10C). Finally, LM11A-31 did not affect the number of cholinergic dystrophic neurite clusters in the cortex, but significantly reduced the total area they occupied as well as the mean area per cluster (Fig. 10D–F). LM11A-31 did not affect any measure in nTg mice. These findings confirmed the ability of LM11A-31 treatment to prevent neurite degeneration in a second mouse model.

Reference: PLoS One. 2014; 9(8): e102136. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4143160/

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.