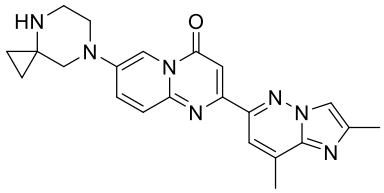
Product data sheet

MedKoo Cat#: 561863 Name: Risdiplam CAS#: 1825352-65-5 Chemical Formula: $C_{22}H_{23}N_7O$ Exact Mass: 401.1964 Molecular Weight: 401.47	
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:
Risdiplam, also known as RG7916 and RO7034067, is a gene splicing modulator (neuromuscular disease).

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	2.0	4.98
Ethanol	2.0	4.98
Water	1.0	2.49

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.49 mL	12.45 mL	24.91 mL
5 mM	0.50 mL	2.49 mL	4.98 mL
10 mM	0.25 mL	1.25 mL	2.49 mL
50 mM	0.05 mL	0.25 mL	0.50 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. Poirier A, Weetall M, Heinig K, Bucheli F, Schoenlein K, Alsenz J, Bassett S, Ullah M, Senn C, Ratni H, Naryshkin N, Paushkin S, Mueller L. Risdiplam distributes and increases SMN protein in both the central nervous system and peripheral organs. Pharmacol Res Perspect. 2018 Nov 29;6(6):e00447. doi: 10.1002/prp2.447. PMID: 30519476; PMCID: PMC6262736.

In vivo study

1. Poirier A, Weetall M, Heinig K, Bucheli F, Schoenlein K, Alsenz J, Bassett S, Ullah M, Senn C, Ratni H, Naryshkin N, Paushkin S, Mueller L. Risdiplam distributes and increases SMN protein in both the central nervous system and peripheral organs. Pharmacol Res Perspect. 2018 Nov 29;6(6):e00447. doi: 10.1002/prp2.447. PMID: 30519476; PMCID: PMC6262736.

7. Bioactivity
Biological target:

Risdiplam (RG7916) is a SMN2 pre-mRNA splicing modifier that increases survival motor neuron (SMN) protein levels.

In vitro activity

Risdiplam showed an average passive permeability in parental LLC-PK1 cells of around 350 nm/s. Similar permeability was observed in L-MDR1, L-Mdra1, M-BCRP, and M-Bcrp cells in the presence of inhibitor. Risdiplam was found not to be a substrate of human

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MDR1 with an ER of 2.2, but a weak substrate of rodent Mdr1a (ER = 3.7). The predicted CSF-to-unbound plasma partition coefficient (pKp,uu) based on the rodent ER and model from is therefore 0.33. Risdiplam was a weak human BCRP substrate with an ER of 3.7 and a strong Bcrp substrate in rodents with an ER of 44.

Reference: Pharmacol Res Perspect. 2018 Dec; 6(6): e00447. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6262736/

In vivo activity

These findings were confirmed while dosing risdiplam: a similar dose-dependent increase in SMN protein levels in brain and muscle (0.1 mg/kg/day: brain 28%, muscle 32%; 1 mg/kg/day, brain 206%, muscle 210%) was observed after 7 days of once daily dosing in SMNΔ7 mice (Study 4, n = 6 or 7 per dose) (Figure 7). Risdiplam also prolonged survival of SMNΔ7 mice (Study 5) when dosed once daily with risdiplam for 219 days. In Study 5, SMN protein level increases were measured relative to SMN levels in heterozygous control animals and a correlation was observed between increase in SMN protein in blood and in brain. In the same study, risdiplam was shown to improve phenotype and motor function, to prolong survival and to increase body weight gain in SMNΔ7 mice.

Reference: Pharmacol Res Perspect. 2018 Dec; 6(6): e00447. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6262736/