

Product Data Sheet

Product Name: Risdiplam (RG7916)

Cat. No.: GC30845

Chemical Properties

Cas. No. 1825352-65-5

SMILES O=C(C=C(C(C=C1C)=NN2C1=NC(C)=C2)N=C3C=C4)N3C=C4N(CCN5)CC65CC6

Formula C22H23N7O M.Wt 401.46

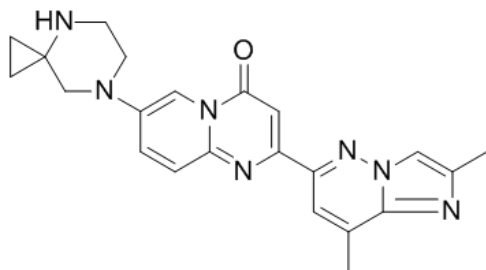
Solubility Ethanol : < 1 mg/mL
(insoluble); DMSO : < 1 mg/mL
(insoluble or slightly soluble)

Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines SMA type I fibroblasts; SMA type I motor neurons

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

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Reaction Conditions 0-1 μ M

Applications Risdiplam (RG7916) was active in vitro in SMA patient-derived fibroblasts and in motor neurons generated from induced pluripotent stem cells (iPSCs) derived from SMA type 1 patient fibroblasts, promoting the inclusion of exon 7, to generate full-length (FL) mRNA.

Animal experiment [1]:

Animal models Adult C/C-allele mice and Neonatal Δ 7 Mouse Model

Preparation Method Adult C/C-allele mice with mild SMA phenotype were treated for 10 days with Risdiplam (RG7916) given once a day orally at three different doses (1, 3, and 10 mg/kg). The level of SMN protein was assessed in brain and in quadriceps muscle. In the Δ 7 mouse model of severe SMA, Risdiplam (RG7916) was administered by intraperitoneal (ip) injection once daily starting on postnatal day (PND) 3 and continued through PND9. The level of SMN protein was assessed in brain and in quadriceps muscle as well.

Dosage form Adult C/C-allele mice : 1, 3, and 10 mg/kg; 10 days; p.o. Δ 7 mouse model : 0-3 mg/kg; 6 days; i.p.

Applications Risdiplam (RG7916) potently increases SMN protein in both brain and muscle tissues of transgenic mouse models of SMA.

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References:

[1]. Ratni H, Ebeling M, et al. Discovery of Risdiplam, a Selective Survival of Motor Neuron-2 (SMN2) Gene Splicing Modifier for the Treatment of Spinal Muscular Atrophy (SMA). J Med Chem. 2018 Aug 9;61(15):6501-6517. doi: 10.1021/acs.jmedchem.8b00741. Epub 2018 Jul 25. PMID: 30044619.

Background

Risdiplam (RG7916) is a small molecule SMN2 pre-mRNA splicing modifier that promotes the inclusion of exon 7 and production of full-length SMN2 mRNA, which can compensate for the loss of SMN1 [1-2].

Risdiplam (RG7916) (0-1 μ M) was active in vitro in SMA patient-derived fibroblasts and in motor neurons generated from induced pluripotent stem cells (iPSCs) derived from SMA type 1 patient fibroblasts, promoting the inclusion of exon 7, to generate full-length (FL) mRNA [1].

Risdiplam (RG7916) potently increases SMN protein in both brain and muscle tissues of transgenic mouse models of SMA [1]. In infants with type 1 spinal muscular atrophy, treatment with oral risdiplam (0.08-0.2 mg/kg/day) led to an increased expression of functional SMN protein in the blood [3].

References:

[1]. Ratni H, Ebeling M, et al. Discovery of Risdiplam, a Selective Survival of Motor Neuron-2 (SMN2) Gene Splicing Modifier for the Treatment of Spinal Muscular Atrophy (SMA). J Med Chem. 2018 Aug 9;61(15):6501-6517. doi: 10.1021/acs.jmedchem.8b00741. Epub 2018 Jul 25. PMID: 30044619.

[2]. Singh RN, Ottesen EW, et al. The First Orally Deliverable Small Molecule for the Treatment of Spinal Muscular Atrophy. Neurosci Insights. 2020 Nov 23;15:2633105520973985. doi: 10.1177/2633105520973985. PMID: 33283185; PMCID: PMC7691903.

[3]. Baranello G, Darras BT, et al. FIREFISH Working Group. Risdiplam in Type 1 Spinal Muscular Atrophy. N Engl J Med. 2021 Mar 11;384(10):915-923. doi: 10.1056/NEJMoa2009965. Epub 2021 Feb 24. PMID: 33626251.

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