Rugonersen

Cat. No.: HY-148130

CAS No.: 2591587-57-2

Molecular Weight: 6530.3

Sequence: DNA, d(P-thio)((2′-O,4′-C-methylene)m5rU-(2′-O,4′-C-methylene)m5rU-(2′-O,4′-C-methylene)rA-C-(2′-O,4′-C-methylene)rA-C-T-T-A-A-T-T-A-T-A-C-T-(2′-O,4′-C-methylene)m5rU-(2′-O,4′-C-methylene)m5rC-(2′-O,4′-C-methylene)m5rC)

Target: E1/E2/E3 Enzyme

Pathway: Metabolic Enzyme/Protease

Storage: -20°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

H_2O : ≥ 100 mg/mL (15.31 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	0.1531 mL	0.7657 mL	1.5313 mL
5 mM	0.0306 mL	0.1531 mL	0.3063 mL
10 mM	0.0153 mL	0.0766 mL	0.1531 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

Rugonersen (RG6091; RO7248824) is a locked-nucleic acid (LNA)- modified antisense oligonucleotides (ASOs), and results in reduction of ubiquitin-protein ligase E3A (UBE3A) silencing. Angelman syndrome (AS) is a severe neurodevelopmental disorder caused by the loss of neuronal E3 ligase UBE3A, Rugonersen has been used for AS reasearch[1][2].

IC_{50} & Target

ubiquitin-protein ligase E3A (UBE3A)[1]

In Vitro

RO7248824 (0-10 μM) show a nanomolar potency against UBE3A-ATS (EC_{50}=26.3 nM), UBE3A mRNA upregulation (EC_{50}=15.4 nM) and UBE3A protein upregulation (EC_{50}=24.8 nM) in Angelman syndrome (AS) neurons[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Rugonersen (RO7248824) (24 mg/monkey; i.t.; for 8-85 d) is well tolerated without adverse in-life effects or tissue pathology and produced a robust, long lasting (up to 3 months) paternal reactivation of UBE3A mRNA/protein across key monkey brain regions[1].

Male cynomolgus monkeys[1]Rugonersen (150 μg; i.c.v.; single dose) selectively and potently reduces UBE3A-ATS, while

concomitantly upregulating the UBE3A mRNA and protein[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male cynomolgus monkey[1]
Dosage:	24 mg per monkey
Administration:	Intrathecal injection; single dose or twice dose with 2 weeks apart; sacrificed at 8, 15, 29, 57, and 85 days after the last dose
Result:	Resulted a long duration of action on paternal UBE3A reactivation in NHP brains after IT delivery.

Animal Model:	WT and AS Ube3a $^{m-/p+}$ mice adult mice (10-12 weeks old)[1]
Dosage:	150 μg per mice
Administration:	Intracerebroventricular injection; single dose; harvested at 2 weeks post injection
Result:	Revealed a steep relationship between UBE3A-ATS knock-down and UBE3A mRNA/protein upregulation, whereby an almost 90% downregulation was needed to achieve a 50% upregulation, respectively.

REFERENCES

[1]. World Health Organization · 2021: WHO Drug Information.

[2]. R Jagasia, et al. Angelman syndrome patient neuron screen identifies a potent and selective clinical ASO targeting UBE3A-ATS with long lasting effect in cynomolgus monkey. bioRxiv, 2022-06-12.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA