

## Eplontersen

<b>Cat. No.:</b>	HY-148089
<b>CAS No.:</b>	1637600-16-8
<b>Molecular Weight:</b>	8606.5
<b>Sequence:</b>	DNA, d([2'-O-(2-methoxyethyl)]m5rU-sp-[2'-O-(2-methoxyethyl)]m5rC-[2'-O-(2-methoxyethyl)]m5rU-[2'-O-(2-methoxyethyl)]m5rU-[2'-O-(2-methoxyethyl)]rG-G-sp-T-sp-T-s p-A-sp-m5C-sp-A-sp-T-sp-G-sp-A-sp-A-sp-[2'-O-(2-methoxyethyl)]rA-[2'-O-(2-methoxyethyl)]m5rU-[2'-O-(2-methoxyethyl)]m5rC-sp-[2'-O-(2-methoxyethyl)]m5rC-sp-[2'-O-(2-methoxyethyl)]m5rC), 5'-[26-[[2-(acetylamino)-2-deoxy-β-D-galactopyranosyl]oxy]-14,14-bis[[3-[[6-[[2-(acetylamino)-2-deoxy-β-D-galactopyranosyl]oxy]hexyl]amino]-3-oxopropoxy]methyl]-8,12,19-trioxo-16-oxa-7,13,20-triazahexacos-1-yl hydrogen phosphate]
<b>Target:</b>	Transthyretin (TTR)
<b>Pathway:</b>	Neuronal Signaling
<b>Storage:</b>	-20°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)

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### SOLVENT & SOLUBILITY

#### In Vitro

H<sub>2</sub>O : 100 mg/mL (11.62 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent	Mass	1 mg	5 mg	10 mg
	Concentration				
	1 mM		0.1162 mL	0.5810 mL	1.1619 mL
	5 mM		0.0232 mL	0.1162 mL	0.2324 mL
	10 mM		0.0116 mL	0.0581 mL	0.1162 mL

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

### BIOLOGICAL ACTIVITY

#### Description

Eplontersen is a triantennary N-acetyl galactosamine (GalNAc<sub>3</sub>-7a)-conjugated antisense oligonucleotide targeting transthyretin (TTR) mRNA to inhibit production of both variant and wild-type TTR protein. Misfolded TTR induces amyloid fibrils formation in the heart and peripheral nerves, leads to amyloid TTR (ATTR) amyloidosis diseases<sup>[1][2][3]</sup>.

#### IC<sub>50</sub> & Target

TTR<sup>[1]</sup>, asialoglycoprotein receptor<sup>[3]</sup>

#### In Vitro

Eplontersen mediates N-acetylgalactosamine moiety targeting the oligonucleotide to cells bearing an asialoglycoprotein receptor<sup>[3]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

<b>In Vivo</b>	Eplontersen (682884) (0.6, 2, 6 mg/kg; s.c.; once a week for 3 weeks) inhibits TTR protein expression in a dose-dependent manner in vivo, without affecting normal growth in transgenic C57BL/6 mice expressing human transthyretin (TTR) <sup>[3]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only.	
	Animal Model:	Transgenic C57BL/6 mice expressing human transthyretin (TTR) (8-week-old) <sup>[3]</sup>
	Dosage:	0.6, 2, 6 mg/kg
	Administration:	Subcutaneous injection; once a week for 3 weeks; performed tail bleeds at various time point; sacrificed mice 72 h following the final administration
	Result:	Decreased TTR mRNA level to 15%, and reduced plasma TTR protein levels to 21% at 6 mg/kg on day 17 after injection. Showed no significant effect on plasma ALT and AST level, no inhibition on body weight, organ weight, spleen weight, and kidney weight as well.

## REFERENCES

- [1]. Aimo A, et al. RNA-targeting and gene editing therapies for transthyretin amyloidosis. *Nat Rev Cardiol.* 2022 Mar 23.
- [2]. Diep JK, et al. Population pharmacokinetic/pharmacodynamic modelling of eplontersen, an antisense oligonucleotide in development for transthyretin amyloidosis. *Br J Clin Pharmacol.* 2022 Jul 22.
- [3]. Prakash Thazha P, et al. Antisense oligonucleotides to hepatitis B virus RNA or transthyretin mRNA conjugated with N-acetylgalactosamine targeting moieties: World Intellectual Property Organization, WO2014179627[P]. 2014-11-06.

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

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