Eplontersen

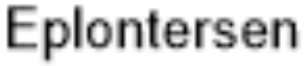
Cat. No.: HY-148089

CAS No.: 1637600-16-8

Target: Transthyretin (TTR)

Pathway: Neuronal Signaling

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Eplontersen is a triantennary N-acetyl galactosamine ($GalNAc_3$-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[1][2][3].
IC_{50} & Target	TTR[1], asialoglycoprotein receptor[3]
In Vitro	Eplontersen mediates N-acetylgalactosamine moiety targeting the oligonucleotide to cells bearing an asialoglycoprotein receptor[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	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)[3]. 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)[3]
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.

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