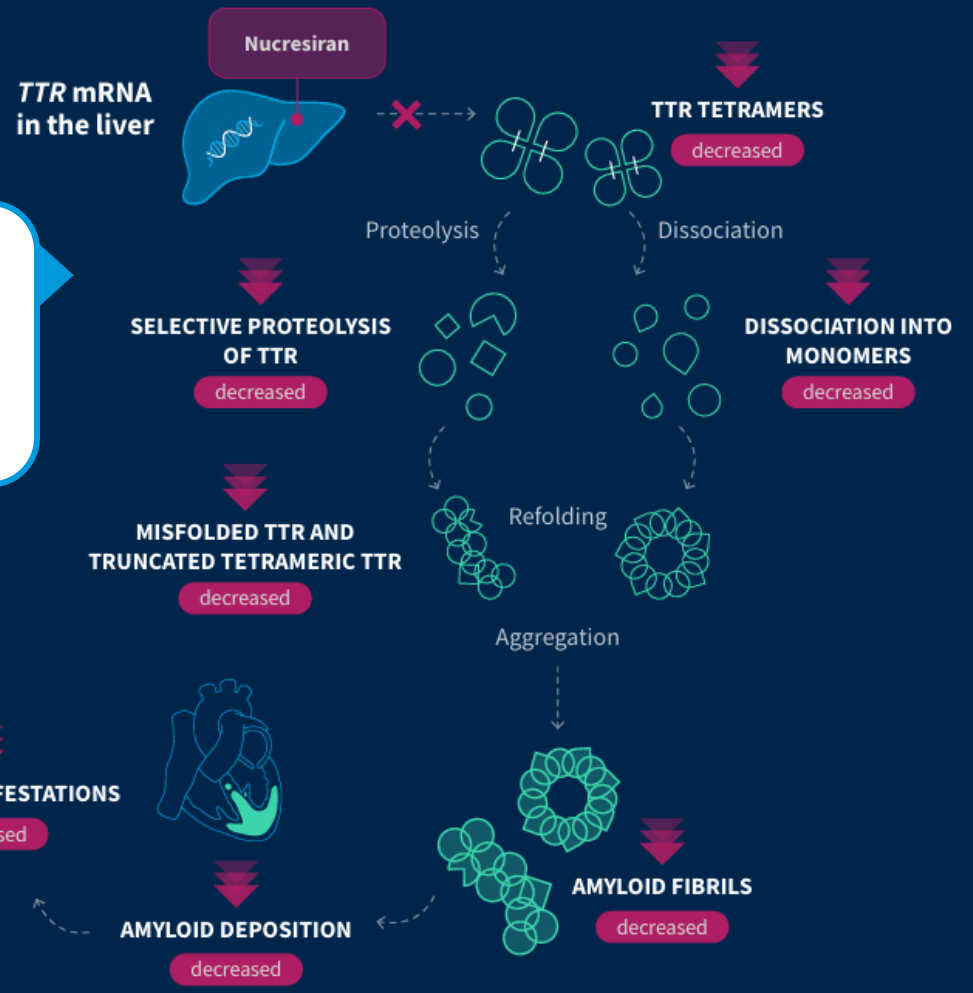
Nucresiran Therapeutic Hypothesis

Target:
Transthyretin (TTR)[1]
siRNA delivery technology:
GalNAc conjugation[1]

TTR is a protein primarily produced in the liver that normally circulates as a tetramer; its normal role is to bind and transport vitamin A and thyroxine (T4) around the body[2,3]



TTR tetramers can dissociate or are cleaved into monomers and other small fragments that misfold and aggregate to form amyloid fibrils that deposit in the myocardium[3-5]

Nucresiran uses RNAi to target TTR mRNA in the liver, reducing the production of TTR[6]

Figure adapted from Porcari A, et al. 2023.[4] GalNAc, N-acetylgalactosamine; mRNA, messenger ribonucleic acid; RNAi, ribonucleic acid interference; TTR, transthyretin. 1. Murad A et al. American Heart Association Hypertension Scientific Sessions, November 16–18, 2024, Chicago, IL, USA. Oral presentation. 2. Griffin JM, et al. Circ Res. 2021;128:1554-1575. 3. Koike H, Katsuno M. Biomedicines. 2019;7:11. 4. Porcari A, et al. Cardiovasc Res. 2023;118:3517-3535. 5. Ibrahim RB, et al. Cell Mol Life Sci. 2020;77:1421-1434. 6. Fontana M, et al. Presented at: Heart Failure 2025; May 17-20, 2025; Belgrade, Serbia.

Alnylam