TRITON-PN hATTR-PN CLINICAL STUDY : Phase 3 Study Design[1]

Randomized, Open-Label Study in Patients with hATTR-PN

Patient Population (N ~ 125)

- Adults (18 – 85 years) diagnosed with hATTR with documented *TTR* mutation
- NIS ≥5 and ≤130
- PND Score ≤IIIb
- Karnofsky performance status ≥60

Select Exclusion Criteria

- NYHA III or IV
- Concurrent tafamidis, acoramidis, or diflunisal (washout required)
- Prior or current TTR lowering treatment or investigational drugs

4:1 RANDOMIZATION

Nucresiran SC Q6M 300 mg

or

Vutrisiran SC Q3M 25 mg

External APOLLO placebo

Primary Endpoint

Change from baseline vs. external placebo in mNIS+7 *(M9)*

Secondary Endpoints

Change from baseline vs. external placebo unless specified:

- Norfolk QoL-DN *(M9, M18)*
- TTR KD vs. vutrisiran *(W6, through M9, through M18)*
- mBMI *(M9, M18)*
- R-ODS *(M18)*
- 10-MWT *(M18)*
- mNIS+7 *(M18)*

Select Exploratory Endpoints

Change from baseline vs. external placebo:

- R-ODS, 10-MWT *(M9)*
- NIS, EQ-5D-5L, FAP, PND, neurofilament light chains
- COMPASS-31
- NT-proBNP and troponin I
- Echocardiographic parameters

Nucresiran SC Q6M 300 mg

Day -42 — **Screening period** — Day 1 (Baseline) — **Treatment period** — Month 18 — **Treatment Extension Period** — Month 36

Efficacy endpoints *(eg. mNIS+7, Norfolk-QoL-DN) will compare nucresiran-treated patients to* ***external control of placebo-treated patients from APOLLO***

Serum TTR reduction *will compare nucresiran-treated patients and in-study vutrisiran-treated patients*

10-MWT: 10-meter walk test; COMPASS-31: Composite Autonomize Symptom Score – 31; EQ-5D-5L: Euro Quality of Life 5 Dimensions 5 Levels; FAP: Familial Amyloid Polyneuropathy; hATTR-PN: hereditary transthyretin amyloidosis with polyneuropathy; KD: knockdown; mBMI: modified Body Mass Index; mNIS+7: modified NIS + 7; NIS: Neuropathy Impairment Score; Norfolk QoL-DN: Norfolk Quality of Life – Diabetic Neuropathy; NT-proBNP: N-terminal pro B-type natriuretic peptide; NYHA: New York Heart Association; PND: Polyneuropathy Disability; Q3M: every-3-months; Q6M: every-6-months; R-ODS: Rasch-built Overall Disability Scale; SC: subcutaneous; TTR: transthyretin. 1. Obici et al. American Academy of Neurology 2026, April 18–22, 2026, Chicago, IL, US. Poster.

Alnylam