

: Phase 3 Study Design¹

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 $\leq$ 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:

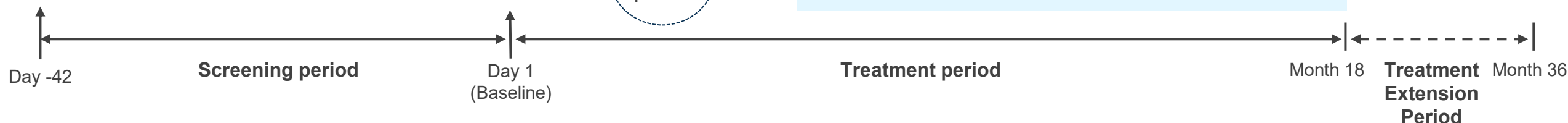
- Norfolk QoL-DN (M9, M18)
- TTR KD vs. vutrisiran (W6, through M9, through M18)
- mBMI (M9, M18)
- R-ODS (M18)
- 10-MWT (M18)
- mNIS+7 (M18)

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



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