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Neurological and Cardiac Improvements With PRX004 in TTR Amyloidosis Patients: Results of a Phase 1 Study

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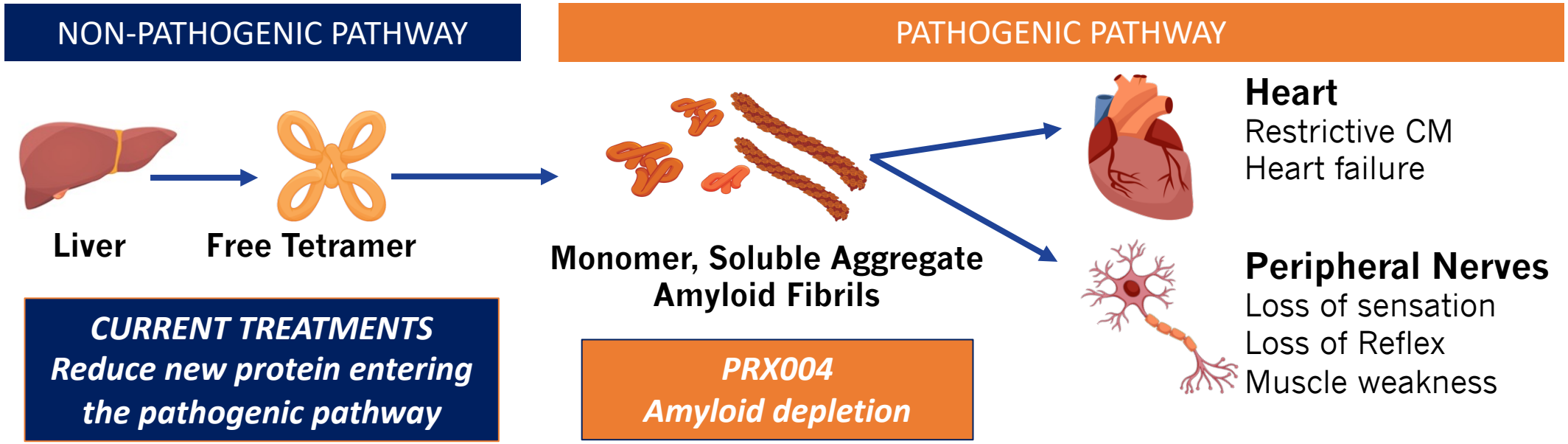
AAN 2021 Virtual Annual Meeting

Disclosures

- Consultant for Alnylam, Akcea, Prothena
- Speakers Bureau for Alnylam, Akcea
- Received research support from Swedish Heart and Lung Foundation

PRX004 MOA and Phase 1 Study Design



PRX004-101 Study Design*

Phase 1 open-label, dose-escalation study with long-term extension phase

DOSE-ESCALATION PHASE
- 3+3 study design
- 6 dose levels (0.1, 0.3, 1, 3, & 10 mg/kg)

IV q28d for 3 months

LONG-TERM EXTENSION PHASE
- Up to 15 additional doses

IV q28d

UNPUBLISHED DATA – DO NOT COPY OR DISTRIBUTE

*ClinicalTrials.gov ID: NCT03336580. ATTR, amyloid transthyretin; CM, cardiomyopathy; IV, intravenous; MOA, mechanism of action; q28, every 28 days

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PRX004 Exposure, PK/PK & Safety

Exposure

- All 21 hATTR subjects received ≥3 PRX004 doses in dose-escalation phase; 17 subjects enrolled in the long-term extension phase
- 223 infusions were given over 21 patients who received between 3-17 infusions through the study.

Pharmacokinetics/Pharmacodynamics:

- PRX004 exposure increased in a dose-proportional manner across all cohorts
- Mean $t_{1/2}$ was similar across cohorts (~31 days)
- PRX004 doses ≥3mg/kg expected to reach exposure to occupy >90% of amyloid

	PRX004 Dose (mg/kg)						
SAEs*	0.1 n=3	0.3 n=3	1 n=3	3 n=3	10 n=3	30 n=6	Total N=21
TR	0	0	0	0	0	0	0
NTR	0	0	2 (1)	0	2 (2)	5 (2)	9 (5)
Death	0	0	0	0	0	0	0

NTR, not treatment related; SAEs, serious treatment-emergent adverse events; TR, treatment-related
*Number of events (number of patients reporting)

Safety:

- There were no drug-related serious AEs, dose-limiting toxicities, or deaths
- Most common AEs (≥10%) were fall, anemia, upper respiratory tract infection, back pain, constipation, diarrhea, and insomnia

- **Dose-proportional increase in PRX004 exposure across all 6 dose level cohorts**
- **PRX004 was safe and well tolerated at all doses tested**

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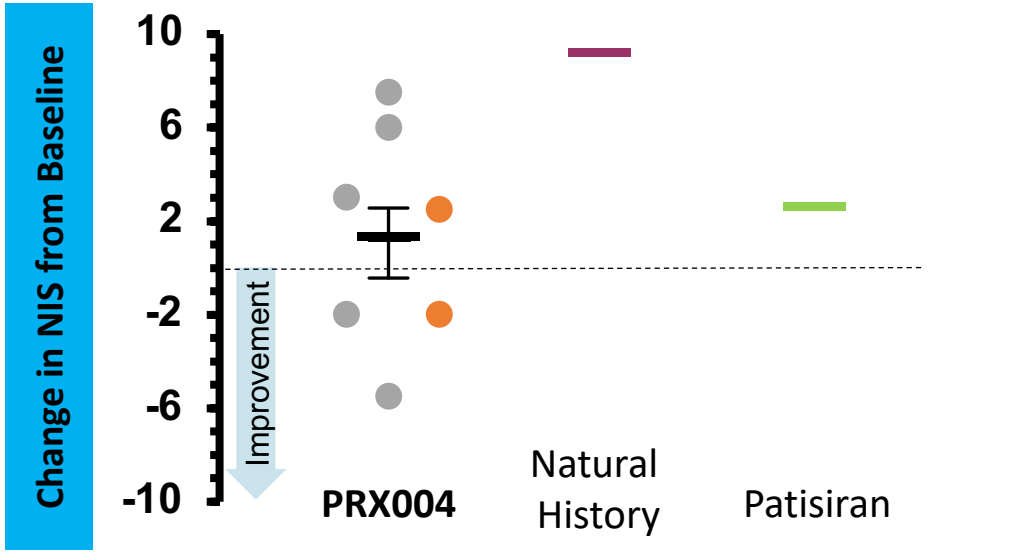
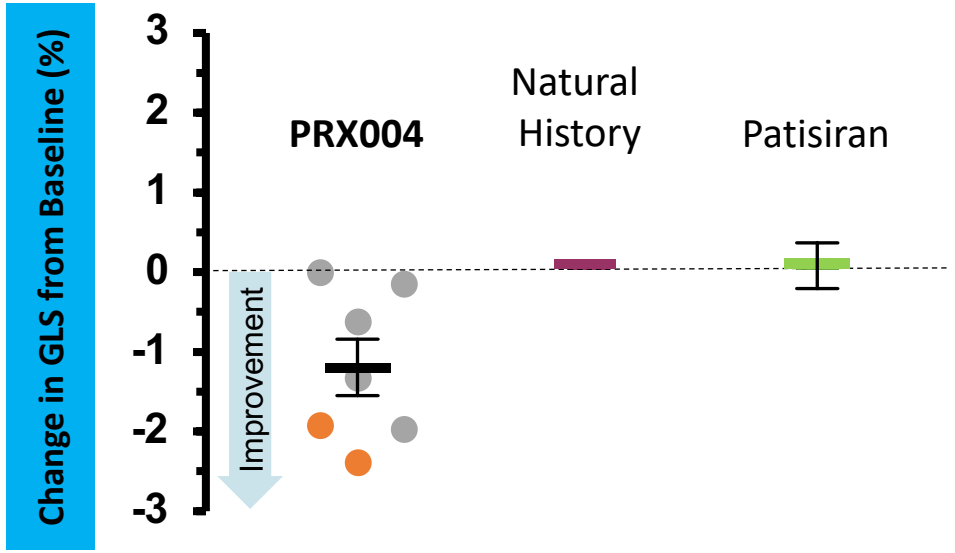
PRX004 Improvement in Neuropathy and Cardiac Systolic Function at Month 9



- NIS change for all 7 patients on PRX004 was more favorable than published data in untreated patients[1,2] (+1.29 vs +9.2) at 9 months
  - For 3 of these 7 patients, NIS change was -3.33
  - In patients on PRX004 alone*, NIS change was 0
- Patients on patisiran[3,4] had a mean NIS change of +2.6 (at 18 months)



- GLS change for all 7 patients on PRX004 was more favorable than data in untreated patients[5] (-1.21% at 9 months vs +1.46% at 18 month).
  - For the 3 patients who improved on NIS, the GLS improvement was more pronounced (-1.51%)
- Patients on patisiran[5] had a mean GLS change of +0.08% (at 18 months)

- **PRX004 improved neuropathy and cardiac function in evaluable patients**
- **These clinical results from a depleter MOA in ATTR amyloidosis suggest that PRX004 may provide a new treatment paradigm for advanced ATTR-cardiomyopathy patients at high risk for early mortality**

*Patients on tafamidis and/or diflunisal were included in the study if dose stable for 6 months. GLS, global longitudinal strain; NIS, neuropathy impairment score.

1. Adams D et al., *Neurology*. 2015;85(8):675-682. 2. Berk JL et al., *JAMA*. 2013;310(24):2658-67. 3Coelho et al. *Orphanet Journal of Rare Diseases,* 2020; 15:179; 4.Onpattro EPAR public assessment report EMA/55462/2018 October 30, 2018. 5.Solomon et al. *Circulation*. 2019;139(4):431-443.

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