Dear Members of the Amyloidosis Community,

Today marks an important day in our pursuit of a meaningful treatment for TTR-Amyloidosis. We are pleased to share the exciting news that we have reported positive top-line results from our NEURO-TTR study of inotersen (IONIS-TTR_{Rx}).

The NEURO-TTR study with familial amyloid polyneuropathy (FAP) met both primary endpoints. Over the 15-month period of the study:

- Inotersen-treated patients achieved a statistically significant benefit compared to placebo in the modified Neuropathy Impairment Score +7 (mNIS+7), ($p<0.0001$).
- Inotersen-treated patients also achieved a statistically significant benefit compared to placebo in the Norfolk Quality of Life Questionnaire -Diabetic Neuropathy (Norfolk QOL-DN), ($p=0.0006$).

In addition, patients treated with inotersen experienced benefit regardless of disease stage (Stage 1 and Stage 2) or TTR mutation (V30M and non-V30M).

Patients treated with inotersen experienced more adverse events than those who were treated with placebo. Two key safety findings related to thrombocytopenia and renal effects were observed during the study that required changes to the monitoring schedule. Enhanced monitoring was implemented during the study to support early detection and management of these issues. A detailed review of safety data from the study is ongoing.

As a result of these positive data, over the coming months we will work closely with the GSK team to submit our marketing applications to regulatory authorities in multiple countries. The marketing applications will include all of the data from the Phase 3 NEURO-TTR data analysis and all other clinical and preclinical data currently available. Patients enrolled in the NEURO-TTR study will be able to continue on treatment in the open-label extension study.

We understand that the key question on peoples' minds will now be one of access. Today our focusing on understanding and analyzing the data we have in hand and the further data that is still pending. We are also prioritizing regulatory filing preparations. We will provide further updates on the program and on our progress.

We would like to sincerely thank the patients participating in our clinical studies, the study doctors who provide exceptional care for these families, and the entire Amyloidosis community, who inspire us to be at our best each and every day. Our respect and admiration for the Amyloidosis community's tireless efforts to advance research and development for an approved treatment grows each and every day. We still have work to do, but this milestone advances us to the next steps in this endeavor. We will continue to share information and program updates to the community when possible and would like to express our deepest appreciation to all involved in this important journey.

Ionis' TTR Amyloidosis Team