SUPPLEMENTAL DATA

Hereditary Transthyretin Amyloidosis: Baseline Characteristics of Patients in the NEURO-TTR Trial

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Supplemental Figure S1: Prevalence of TTR Mutations in the NEURO-TTR Trial. Number and percentage of patients (N=172) exhibiting each observed mutation. Val30Met (52%) was the most common TTR mutation, followed by Thr60Ala (13%). Mutations categorized under Others were each represented by one patient.
**Supplemental Figure S2:** Symptoms Dysfunction by PND Score. Presence of symptoms as measured by NSC score becomes increasingly broader as disease stage (PND score) progresses. (A) PND I (N=55). (B) PND II (N=61). (C) PND III/IV (N=56). Chart labels show symptom categories, number of subjects, percentage subjects. Symptom categories are as follows: Muscle weakness (W), sensory loss (S), Positive neuropathy sensory symptoms (P), and autonomic (A).
Supplemental Table S1: Baseline Laboratory Tests by Region, Disease Onset, and Prior Treatment with TTR Stabilizers

|                      | Total (n=172) | Region | Disease Onset | Prior Treatment |
|----------------------|--------------|--------|---------------|-----------------|
|                      |              | US (n=82) | Europe (n=60) | SA (n=30)       | Early (n=56) | Late (n=116) | Stabilizers (n=99) | Naïve (n=73) |
| **SERUM CHEMISTRY**  |              |         |               |                 |               |             |                  |              |
| Albumin (g/L)        |              |         |               |                 |               |             |                  |              |
| Mean (SD)            | 42.6 (3.3)   | 42.9 (2.6) | 42.3 (3.6) | 42.1 (4.3) | 42.8 (3.9) | 42.5 (3.0) | 42.9 (3.2) | 42.2 (3.4) |
| Median               | 42.7         | 43.2     | 42.1         | 42.5         | 42.7         | 42.7         | 43.0         | 42.3         |
| (Min – Max)          | (32-50)      | (35-48)  | (32-50)      | (32-48)      | (32-50)      | (32-49)      | (32-50)      | (32-48)      |
| Creatine Kinase (U/L)|              |         |               |                 |               |             |                  |              |
| Mean (SD)            | 196.6 (123.4)| 196.2 (115.8)| 193.4 (118.2)| 204.1 (154.6)| 208.6 (136.9)| 190.8 (116.6)| 204.5 (128.6)| 185.9 (116.2)|
| Median               | 171.2        | 171.8    | 187.8        | 162.0        | 181.5        | 168.9        | 173.3        | 163.3        |
| (Min – Max)          | (40-689)     | (47-536) | (40-557)     | (51-689)     | (43-689)     | (40-544)     | (40-689)     | (43-536)     |
| Creatinine (µmol/L)  |              |         |               |                 |               |             |                  |              |
| Mean (SD)            | 76.6 (19.1)  | 80.6 (20.2)| 71.0 (16.8) | 76.6 (18.2)| 72.4 (14.3) | 78.6 (20.8)| 76.8 (18.6)| 76.2 (19.9)|
| Median               | 74.3         | 77.0     | 70.3         | 80.0         | 74.3         | 74.7         | 75.0         | 73.0         |
| (Min – Max)          | (38-142)     | (43-142)| (38-124)     | (43-122)     | (43-101)     | (38-142)     | (38-142)     | (43-122)     |
| eGFR (mL/min/1.72m²) |              |         |               |                 |               |             |                  |              |
| Mean (SD)            | 88.4 (18.6)  | 82.7 (17.5)| 93.8 (17.6)| 93.0 (19.4)| 100.4 (16.3)| 82.6 (16.8)| 88.2 (18.3)| 88.7 (19.1)|
| Median               | 89.3         | 86.5     | 95.5         | 95.3         | 101.8        | 85.8         | 89.0         | 90.3         |
| (Min – Max)          | (41-133)     | (41-123)| (52-133)     | (53-126)     | (59-133)     | (41-124)     | (42-133)     | (41-126)     |
| Region       | Disease Onset | Prior Treatment |
|--------------|---------------|-----------------|
| Total (n=172)|               |                 |
| US (n=82)    |               |                 |
| Europe (n=60)|               |                 |
| SA (n=30)    |               |                 |
| Early (n=56) |               |                 |
| Late (n=116) |               |                 |
| Stabilizers  |               |                 |
| Naïve (n=73) |               |                 |

### HEMATOLOGY

**Platelets (10^9/L)**

| Region       | Disease Onset | Prior Treatment |
|--------------|---------------|-----------------|
| Total (n=172)|               |                 |
| US (n=82)    |               |                 |
| Europe (n=60)|               |                 |
| SA (n=30)    |               |                 |
| Early (n=56) |               |                 |
| Late (n=116) |               |                 |
| Stabilizers  |               |                 |
| Naïve (n=73) |               |                 |

| Region       | Disease Onset | Prior Treatment |
|--------------|---------------|-----------------|
| US (n=82)    |               |                 |
| Europe (n=60)|               |                 |
| SA (n=30)    |               |                 |
| Early (n=56) |               |                 |
| Late (n=116) |               |                 |
| Stabilizers  |               |                 |
| Naïve (n=73) |               |                 |

**Red Blood Cell Count (10^12/L)**

| Region       | Disease Onset | Prior Treatment |
|--------------|---------------|-----------------|
| Total (n=172)|               |                 |
| US (n=82)    |               |                 |
| Europe (n=60)|               |                 |
| SA (n=30)    |               |                 |
| Early (n=56) |               |                 |
| Late (n=116) |               |                 |
| Stabilizers  |               |                 |
| Naïve (n=73) |               |                 |

**Hemoglobin (g/L)**

| Region       | Disease Onset | Prior Treatment |
|--------------|---------------|-----------------|
| Total (n=172)|               |                 |
| US (n=82)    |               |                 |
| Europe (n=60)|               |                 |
| SA (n=30)    |               |                 |
| Early (n=56) |               |                 |
| Late (n=116) |               |                 |
| Stabilizers  |               |                 |
| Naïve (n=73) |               |                 |

### OTHER SERUM LAB TESTS

**RBP4 (µg/mL)**

| Region       | Disease Onset | Prior Treatment |
|--------------|---------------|-----------------|
| Total (n=172)|               |                 |
| US (n=82)    |               |                 |
| Europe (n=60)|               |                 |
| SA (n=30)    |               |                 |
| Early (n=56) |               |                 |
| Late (n=116) |               |                 |
| Stabilizers  |               |                 |
| Naïve (n=73) |               |                 |

**Vitamin A (µg/dL)**
|                                | Total (n=172) | US (n=82) | Europe (n=60) | SA (n=30) | Early (n=56) | Late (n=116) | Stabilizers (n=99) | Naïve (n=73) |
|--------------------------------|---------------|-----------|---------------|-----------|--------------|--------------|-------------------|--------------|
| **Region**                     |               |           |               |           |              |              |                   |              |
| **Disease Onset**              |               |           |               |           |              |              |                   |              |
| Mean (SD)                      | 51.1 (15.4)   | 46.8 (14.1)| 55.0 (16.0)   | 54.9 (15.4)| 53.2 (15.9)  | 50.0 (15.2)  | 52.7 (14.6)       | 48.9 (16.3)  |
| Median                         | 50.8          | 47.5      | 54.3          | 52.8      | 52.0         | 50.0         | 52.5              | 47.0         |
| (Min – Max)                    | (13-92)       | (13-87)   | (25-92)       | (24-91)   | (13-91)      | (23-92)      | (13-92)           | (24-91)      |
| **hsCRP (mg/L)**               |               |           |               |           |              |              |                   |              |
| Mean (SD)                      | 3.78 (11.07)  | 2.26 (3.99)| 3.63 (8.79)   | 8.17 (22.21)| 6.07 (17.23) | 2.65 (5.91)  | 3.99 (12.53)      | 3.47 (8.64)  |
| Median                         | 0.90          | 0.90      | 0.90          | 0.80      | 0.80         | 0.90         | 0.90              | 0.90         |
| (Min – Max)                    | (0.2-105.0)   | (0.2-24.6)| (0.2-51.4)    | (0.2-105.0)| (0.2-105.0)  | (0.2-105.0)  | (0.2-105.0)       | (0.2-64.6)   |
| **URINALYSIS**                 |               |           |               |           |              |              |                   |              |
| Protein Excretion Rate (mg/day)|               |           |               |           |              |              |                   |              |
| Mean (SD)                      | 165.9 (172.4) | 144.6 (147.4)| 176.1 (185.9)| 194.0 (196.8)| 183.6 (202.4)| 157.3 (156.1)| 169.0 (168.0)     | 162.2 (178.8)|
| Median                         | 110.0         | 103.5     | 112.0         | 138.5     | 120.0        | 107.5        | 109.0             | 114.0        |
| (Min – Max)                    | (44-936)      | (44-884)  | (46-936)      | (60-912)  | (46-936)     | (44-884)     | (44-936)          | (49-912)     |
| A/C (mg/mmol)                  |               |           |               |           |              |              |                   |              |
| Mean (SD)                      | 5.84 (14.11)  | 5.10 (15.81)| 5.52 (10.54) | 8.32 (16.60)| 8.78 (18.03) | 4.35 (11.47) | 4.48 (9.40)       | 7.76 (18.79) |
| Median                         | 1.24          | 1.13      | 1.47          | 0.90      | 1.13         | 1.24         | 1.24              | 1.24         |
| (Min – Max)                    | (0.23-91.76)  | (0.33-91.76)| (0.45-53.22) | (0.23-60.23)| (0.23-91.76) | (0.33-88.82) | (0.34-53.22)      | (0.23-91.76) |
| P/C (mg/mmol)                  |               |           |               |           |              |              |                   |              |
| Mean (SD)                      | 21.23 (28.48) | 18.84 (29.25)| 21.26 (23.42)| 27.73 (34.89)| 25.51 (30.34)| 19.17 (27.43)| 18.46 (19.91)     | 25.00 (36.90)|
| Median                         | 12.83         | 12.33     | 14.33         | 14.33     | 13.05        | 12.33        | 12.67             | 13.11        |
| Region     | Disease Onset | Prior Treatment |
|------------|--------------|----------------|
| Total (n=172) | US (n=82) | Europe (n=60) | SA (n=30) | Early (n=56) | Late (n=116) | Stabilizers (n=99) | Naïve (n=73) |
| (Min – Max) | (5.50-205.67) | (5.50-205.67) | (6.67-152.00) | (6.33-168.33) | (5.50-205.67) | (5.50-152.00) | (6.67-205.67) |

US denotes United States; SA, South America/Australasia.

Lab Test (LLN-ULN): Albumin, serum (35-55 g/L); Creatine Kinase (25-210 U/L); Creatinine, serum (44-124 μmol/L); eGFR (CKD-EPI formula) (>60 mL/min/1.73m²); Platelets (140-400 10⁹/L); Red Blood Cell Count (RBCs) (4.30-6.00 10¹²/L); Hemoglobin (136-180 g/L); Retinol Binding Protein 4 (RBP4) (11.9-48.3 μg/mL); Vitamin A (24-128 ug/dL); High-sensitivity C-reactive protein (hsCRP) (0-3 mg/L); Protein Excretion Rate, urine (0-299 mg/day); Albumin/Creatinine Ratio (A/C) (0-1.8 mg/mmol); Protein/Creatinine Ratio (P/C) (0-23 mg/mmol).
## Supplemental Table S2. Baseline Laboratory Tests by TTR Mutation (≥5% Prevalence in NEURO-TTR)

|                     | Total (n=172) | Val30Met (n=89) | Non-Val30Met (n=83) | Thr60Ala (n=22) | Leu58His (n=10) | Ser77Tyr (n=9) | Phe64Leu (n=8) |
|---------------------|--------------|-----------------|---------------------|----------------|----------------|---------------|---------------|
| **SERUM CHEMISTRY** |              |                 |                     |                |                |               |               |
| Albumin (g/L)       |              |                 |                     |                |                |               |               |
| Mean (SD)           | 42.6 (3.3)   | 42.5 (3.8)      | 42.7 (2.8)          | 41.7 (3.1)     | 44.1 (2.4)     | 43.2 (2.6)    | 43.8 (3.0)    |
| Median              | 42.7         | 42.7            | 42.7                | 42.3           | 44.8           | 42.7          | 44.0          |
| (Min – Max)         | (32-50)      | (32-50)         | (35-49)             | (35-47)        | (39-47)        | (40-49)       | (38-48)       |
| Creatine Kinase (U/L)|              |                 |                     |                |                |               |               |
| Mean (SD)           | 196.6 (123.4)| 220.5 (137.1)  | 170.9 (101.6)       | 129.9 (63.9)   | 181.8 (137.4)  | 119.0 (43.7)  | 233.7 (121.3) |
| Median              | 171.2        | 202.0           | 158.3               | 115.7          | 136.7          | 107.0         | 243.5         |
| (Min – Max)         | (40-689)     | (40-689)        | (47-536)            | (50-279)       | (64-448)       | (69-173)      | (92-386)      |
| Creatinine (µmol/L)|              |                 |                     |                |                |               |               |
| Mean (SD)           | 76.6 (19.1)  | 78.4 (18.7)     | 74.6 (19.4)         | 80.3 (18.7)    | 74.0 (17.4)    | 67.5 (16.0)   | 72.0 (15.6)   |
| Median              | 74.3         | 77.3            | 71.0                | 77.7           | 76.3           | 63.3          | 70.7          |
| (Min – Max)         | (38-142)     | (43-124)        | (38-124)            | (53-120)       | (43-103)       | (39-94)       | (55-105)      |
| eGFR (mL/min/1.73m²)|              |                 |                     |                |                |               |               |
| Mean (SD)           | 88.4 (18.6)  | 89.5 (19.9)     | 87.2 (17.2)         | 82.3 (16.6)    | 85.1 (12.1)    | 91.7 (15.1)   | 89.0 (13.3)   |
| Median              | 89.3         | 90.0            | 89.0                | 83.8           | 88.0           | 94.0          | 89.3          |
| (Min – Max)         | (41-133)     | (48-133)        | (41-124)            | (42-109)       | (62-98)        | (57-108)      | (62-108)      |

## HEMATOLOGY
|                  | Total (n=172) | Val30Met (n=89) | Non-Val30Met (n=83) | Thr60Ala (n=22) | Leu58His (n=10) | Ser77Tyr (n=9) | Phe64Leu (n=8) |
|-----------------|--------------|-----------------|---------------------|-----------------|-----------------|----------------|---------------|
| **Platelets (10^9/L)** |              |                 |                     |                 |                 |                |               |
| Mean (SD)       | 219.5 (56.1) | 228.8 (57.1)    | 209.5 (53.5)        | 210.8 (60.7)    | 226.4 (39.3)    | 205.5 (59.4)   | 203.2 (56.1)   |
| Median          | 215.8        | 225.5           | 201.0               | 192.0           | 229.5           | 186.5          | 201.8         |
| (Min – Max)     | (117-406)    | (123-387)       | (117-406)           | (133-406)       | (159-273)       | (150-338)      | (117-276)      |
| **RBCs (10^12/L)** |              |                 |                     |                 |                 |                |               |
| Mean (SD)       | 4.489 (0.511)| 4.529 (0.534)   | 4.446 (0.483)       | 4.370 (0.617)   | 4.728 (0.433)   | 4.466 (0.390)  | 4.574 (0.540)  |
| Median          | 4.500        | 4.565           | 4.450               | 4.333           | 4.665           | 4.430          | 4.695         |
| (Min – Max)     | (3.16-6.31)  | (3.20-6.31)     | (3.16-5.41)         | (3.16-5.41)     | (4.16-5.38)     | (3.77-5.15)    | (3.46-5.09)    |
| **Hemoglobin (g/L)** |              |                 |                     |                 |                 |                |               |
| Mean (SD)       | 136.6 (14.2) | 136.4 (14.3)    | 136.8 (14.1)        | 135.8 (16.1)    | 145.9 (14.8)    | 136.7 (12.1)   | 137.4 (17.3)   |
| Median          | 137.2        | 137.5           | 137.0               | 138.3           | 142.7           | 135.5          | 143.5         |
| (Min – Max)     | (97-181)     | (97-181)        | (103-165)           | (106-164)       | (124-165)       | (120-158)      | (103-156)      |
| **OTHER SERUM LAB TESTS** |              |                 |                     |                 |                 |                |               |
| **RBP4 (µg/mL)**|              |                 |                     |                 |                 |                |               |
| Mean (SD)       | 35.49 (10.49)| 39.91 (8.89)    | 30.75 (10.04)       | 32.00 (11.46)   | 36.29 (6.31)    | 32.56 (13.24)  | 28.83 (6.37)   |
| Median          | 34.79        | 40.01           | 28.27               | 28.22           | 37.24           | 30.42          | 28.05         |
| (Min – Max)     | (10.96-64.21)| (15.01-63.11)   | (10.96-64.21)       | (13.88-57.38)   | (26.67-42.85)   | (15.86-64.21)  | (21.33-40.76)  |
| **Vitamin A (µg/dL)** |              |                 |                     |                 |                 |                |               |
| Mean (SD)       | 51.1 (15.4)  | 58.2 (14.0)     | 43.4 (13.1)         | 43.7 (14.0)     | 51.9 (8.9)      | 44.8 (17.2)    | 40.5 (7.3)     |
|                     | Total (n=172) | Val30Met (n=89) | Non-Val30Met (n=83) | Thr60Ala (n=22) | Leu58His (n=10) | Ser77Tyr (n=9) | Phe64Leu (n=8) |
|---------------------|---------------|-----------------|---------------------|-----------------|-----------------|---------------|---------------|
| **Median**          | 50.8          | 56.5            | 42.5                | 42.0            | 50.3            | 39.5          | 41.0          |
| (Min – Max)         | (13-92)       | (24-92)         | (13-85)             | (23-80)         | (41-68)         | (25-85)       | (31-53)       |
| **hsCRP (mg/L)**    |               |                 |                     |                 |                 |               |               |
| **Mean (SD)**       | 3.78 (11.07)  | 4.78 (13.94)    | 2.71 (6.74)         | 2.59 (3.64)     | 4.42 (7.90)     | 6.29 (16.92)  | 1.76 (1.05)   |
| **Median**          | 0.90          | 1.00            | 0.70                | 0.80            | 0.90            | 0.60          | 1.90          |
| (Min – Max)         | (0.2-105.0)   | (0.2-105.0)     | (0.2-51.4)          | (0.2-13.1)      | (0.2-24.6)      | (0.2-51.4)    | (0.2-3.1)     |
| **URINALYSIS**      |               |                 |                     |                 |                 |               |               |
| **Protein Excretion Rate (mg/day)** |             |                 |                     |                 |                 |               |               |
| **Mean (SD)**       | 165.9 (172.4) | 185.4 (186.5)   | 141.0 (150.2)       | 129.3 (106.9)   | 84.5 (17.1)     | 104.3 (70.8)  | 263.6 (347.1) |
| **Median**          | 110.0         | 120.0           | 94.0                | 102.0           | 81.0            | 83.0          | 111.0         |
| (Min – Max)         | (44-936)      | (46-936)        | (44-884)            | (44-540)        | (68-108)        | (60-273)      | (90-884)      |
| **A/C (mg/mmol)**   |               |                 |                     |                 |                 |               |               |
| **Mean (SD)**       | 5.84 (14.11)  | 7.29 (13.34)    | 4.22 (14.85)        | 1.79 (2.02)     | 0.90 (0.57)     | 1.61 (1.36)   | 13.32 (33.29) |
| **Median**          | 1.24          | 1.64            | 0.96                | 1.02            | 0.74            | 1.13          | 0.57          |
| (Min – Max)         | (0.23-91.76)  | (0.23-60.23)    | (0.33-91.76)        | (0.33-9.61)     | (0.34-2.03)     | (0.57-4.63)   | (0.57-88.82)  |
| **P/C (mg/mmol)**   |               |                 |                     |                 |                 |               |               |
| **Mean (SD)**       | 21.23 (28.48) | 23.80 (28.30)   | 18.48 (28.58)       | 15.44 (10.86)   | 11.08 (3.40)    | 12.22 (4.73)  | 34.33 (69.25) |
| **Median**          | 12.83         | 14.00           | 12.33               | 13.22           | 10.83           | 11.67         | 10.33         |
| (Min – Max)         | (5.50-205.67) | (5.67-168.33)   | (5.50-205.67)       | (5.50-59.50)    | (6.50-18.00)    | (7.00-20.33)  | (6.67-205.67) |
|                      | Total (n=172) | Val30Met (n=89) | Non-Val30Met (n=83) | Thr60Ala (n=22) | Leu58His (n=10) | Ser77Tyr (n=9) | Phe64Leu (n=8) |
|----------------------|--------------|----------------|---------------------|----------------|----------------|----------------|----------------|
| Lab Test (LLN-ULN):  |              |                |                     |                |                |                |                |
| Albumin, serum       |              |                |                     |                |                |                |                |
| Creatinine, serum    |              |                |                     |                |                |                |                |
| eGFR (CKD-EPI formula)|              |                |                     |                |                |                |                |
| Platelets            |              |                |                     |                |                |                |                |
| Red Blood Cell Count |              |                |                     |                |                |                |                |
| Hemoglobin           |              |                |                     |                |                |                |                |
| Retinol Binding      |              |                |                     |                |                |                |                |
| Vitamin A            |              |                |                     |                |                |                |                |
| High-sensitivity     |              |                |                     |                |                |                |                |
| Protein Excretion Rate, urine | |                |                     |                |                |                |                |
| Albumin/Creatinine Ratio (A/C) | |                |                     |                |                |                |                |
| Protein/Creatinine Ratio (P/C) | |                |                     |                |                |                |                |