**Supplemental Table I. Intravenous Administration of AAVrh.10hFXN to MCK Mice with Assessment of FXN Levels, Heart Function and Survival[1]**

| Group | Mouse strain[2] | Treatment[3] | n | Vector dose (gc/kg) | Assessments[4,5,6,7] |
|---|---|---|---|---|---|
| 1 | MCK-FXN cKO | AAVrh.10hFXN | 10M/10F | $1.8x10^{11}$ | Body weights[4]<br>Echocardiogram[5]<br>Survival[6]<br>FXN expression in heart [7] |
| 2 | MCK-FXN cKO | AAVrh.10hFXN | 10M/10F | $5.7x10^{11}$ | |
| 3 | MCK-FXN cKO | AAVrh.10hFXN | 10M/10F | $1.8x10^{12}$ | |
| 4 | MCK-FXN cKO | PBS | 7M/9F | None | |
| 5 | C57Bl/6 | None | 5M/5F | None | |

[1] AAVrh.10hFXN vector administered intravenously at day 0 of the study to 7-wk old MCK mice, at 1 of 3 doses (n=10F/10M per dose). Controls are MCK mice that received PBS (7M/9F) and untreated C57Bl/6 (wild type, WT) controls (5M/5F) as comparators for the efficacy study. To avoid potential study bias, all mice were randomly assigned to cohort groups, with staggered dosing of animals across all groups.

[2] Obtained from Jackson Labs; stock #28520; re-genotyped to confirm status.

[3] The vector is a serotype rh.10 adeno-associated virus (AAV) encoding a human frataxin (FXN) gene under control of CAG promoter (AAVrh.10hFXN) and is tested for endotoxin and sterility. Treatment (vector, PBS, or none) was administered on day 0 by the intravenous (IV) tail vein route, 0.1 ml volume.

[4] Body weight (groups 1-4) were obtained 1 wk prior to therapy, on the day of dosing, daily the first week after dosing, and weekly thereafter until the following criteria are met. When any mouse in a group displayed signs of a reduced level of locomotion, hunched posture, or labored breathing (in comparison to healthy C57Bl/6 mice), the entire group was weighed 3 times per week and provided with supportive care as needed. Body weight was also recorded on the day of euthanasia (terminal body weight).

[5] Echocardiograms were performed using ultrasound imaging (Vevo-3100 unit) at 2, 4, 8, and 12 wk post-treatment on a subset (5M/5F) of the mice from each cohort. Pre-treatment echocardiograms were performed at 6 weeks of age (1-wk pre-AAV treatment).

[6] Animals were sacrificed when moribund. Efficacy assessments (echocardiograms on a subset, see footnote 5) and human frataxin protein expression (ELISA) from heart was assessed at sacrifice. PBS controls were sacrificed when moribund and were also used for efficacy (in-life) and expression data comparison at sacrifice. C57Bl/6 mice were only used as controls for the efficacy arm of the study (echo) and sacrificed at endpoints matching the MCK mice survival.

[7] At sacrifice, (except the C57Bl/6 controls, which were sacrificed with no tissue collection), transcardial perfusion with chilled 1x PBS was followed by necropsy with collection of the heart tissue for assessment of human frataxin protein expression (ELISA).