**Supplementary Table 1**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | *Non-Naïve only* | *Non-Naïve only* |  |  |  |  |  |  |  |  |
| Patient information and informed consent process | X |  | X1 |  |  |  |  |  |  |  |
| Inclusion / exclusion criteria | X |  | X1 |  |  |  |  | X |  |  |
| Patient demographics (in accordance with local regulations) | X |  | X1 |  |  |  |  |  |  |  |
| Patient weight (only) | X |  |  |  |  |  |  |  |  |  |
| Vital signs | X |  | X | X | X | X | X | X |  | X |
| Physical Examination (including weight) |  |  |  | X |  | X |  | X |  | X |
| Confirmation prohibited medications have not been used in the past 42 days at Visit 1/since Visit 1 for Visit 2 |  |  | X | X |  |  |  |  |  |  |
| Confirmation prohibited medications have been used within past 42 days/ classify patient as “non-naïve” | X |  |  |  |  |  |  |  |  |  |
| Blinded Randomization |  |  |  | X |  |  |  |  |  |  |
| Relevant medical history | X |  | X1 |  |  |  |  |  |  |  |
| 60-Day drug history | X |  | X1 |  |  |  |  |  |  |  |
| Medication History: Confirm if N-Acetyl-Leucine ever used | X |  | X1 |  |  |  |  |  |  |  |

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Documentation of therapy / concomitant medication | X |  | X | X | X | X | X | X | X | X |
| 12-lead electrocardiogram (ECG) |  |  | X |  | X |  | X |  |  | X |
| Urine Test for N-Acetyl-D-Leucine |  |  | X7 | X | X | X | X | X |  | X |
| Blood safety laboratory tests |  |  | X | X | X | X | X | X |  | X |
| Blood draw for sparse PK |  |  |  | X |  | X |  | X |  | X |
| Blood draw for research purposes |  |  |  | X |  | X |  | X |  | X |
| Follicle stimulating hormone serum |  |  | X |  |  |  |  |  |  |  |
| Urinalysis |  |  | X | X | X | X | X | X |  | X |
| Serum bHCG/pregnancy (if applicable) |  |  | X |  |  |  |  |  |  |  |
| Urine by dipstick for pregnancy test |  |  |  | X | X | X | X | X |  | X |

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Quality of Life EQ-5D-5L for patients aged ≥18 years; EQ-5D-Y for children aged <18 years |  |  | X | X | X | X | X | X |  | X |
| Niemann-Pick type C Clinical Severity Scale (NPC-CSS) |  |  |  | X |  | X |  | X |  | X |
| Scale for Ataxia Rating (SARA) | X |  | X | X | X | X | X | X |  | X |
| Modified Disabling Rating Score (mDRS) |  |  | X | X | X | X | X | X |  | X |
| Scale for Spinocerebellar Ataxia Functional Index (SCAFI) | X |  | X | X | X | X | X | X |  | X |
| Clinical Global Impression of Severity (CGI-S) by Physician / Caregiver/ Patient |  |  | X | X | X | X | X | X |  | X |
| Clinical Global Impression of Change (CGI-I) by Physician / Caregiver/ Patient |  |  |  |  |  | X |  | X |  | X |
| Exit Interview |  |  |  |  |  |  |  | X |  |  |
| Documentation of AEs | X |  | X | X | X | X | X | X | X | X |
| Dispensing of study drug |  |  |  | X | X15 | X | X15 |  |  |  |
| Intake of study drug at site |  |  |  | X16 |  | X |  |  |  |  |
| Return of study drug |  |  |  |  | X | X | X | X |  | X |
| Study drug compliance check |  |  |  |  | X | X | X | X |  | X |

1 Naïve patients only

**Supplementary Table 2**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Patient information and informed consent process | X |  |  |  |  |  |  |
| Inclusion / exclusion criteria | X |  |  |  |  |  |  |
| Physical Examination (+weight) | X |  | X |  | X | X | X |
| Documentation of concomitant medication | X |  | X |  | X | X | X |
| Documentation of frequency of therapy (hours per week) / concomitant medications | X |  | X |  | X | X | X |
| Vital signs | X |  | X |  | X | X | X |
| 12-lead electrocardiogram (ECG) |  |  |  |  | X |  | X |
| Blood safety laboratory tests | X |  | X |  | X | X | X |
| PK Blood Sampling |  | X |  |  | X |  |  |
| Blood Draw for Research Purposes | X |  |  |  | X |  | X |
| Urinalysis | X |  | X |  | X | X | X |
| Urine by dipstick for pregnancy test | X |  | X |  | X | X | X |
| Urine test for N-Acetyl-D-Leucine | X |  |  |  |  | X | X |
| Quality of Life EQ-5D-5L for patients aged ≥18; EQ-5D-Yfor children aged <18 years | X |  | X | X |  | X | X |
| Scale for Ataxia Rating (SARA) | X |  | X | X |  | X | X |
| Niemann-Pick Disease type C Clinical Severity Scale | X |  | X | X |  | X | X |
| Clinical Global Impression of Severity (CGI-S) by Physician / Caregiver (if applicable)/ Patient (if able) | X |  | X | X |  | X | X |
| Documentation of AEs | X | X | X | X | X | X | X |
| Dispensing of study drug |  | X | X |  |  |  |  |
| Intake of study drug at site |  | X |  |  | X |  |  |
| Return of study drug |  |  | X |  | X |  | X |
| Study drug compliance check |  |  | X |  | X |  | X |