TABLES, LISTINGS AND FIGURES

List of outputs and mock shells

Protocol GWEP1447

EudraCT Number: 2015-002939-18

A PHASE 2, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED PHARMACOKINETIC TRIAL IN TWO PARALLEL GROUPS TO INVESTIGATE POSSIBLE DRUG-DRUG INTERACTIONS BETWEEN STIRIPENTOL OR VALPROATE AND GWP42003-P IN PATIENTS WITH EPILEPSY

|  |  |
| --- | --- |
| **Protocol Number: (Version Date)** | GWEP1447  Version 4 (26-Jul-2016)  Version 3 (25-Jul-2016) (Sweden Only)  Version 5 (28-Jul-2016) (France only) |
| **Name of Test Drug:** | Cannabidiol (GWP42003-P) |
| **Phase:** | 2 |
| **Methodology:** | Double-Blind, Randomized, Placebo-Controlled |
| **Sponsor:** | GW Research Ltd  Sovereign House, Vision Park,  Chivers Way,  Histon, Cambridge  CB24 9BZ,  Tel: +44 (0) 1223 266800, Fax: +44 (0) 1223 235667 |
| **Sponsor Representative:** | Daniel Checketts Head of Biometrics |
| **Document Date:** | 13 April 2017 |
| **Document Version:** | 0.1 |

# **INTRODUCTION**

All outputs (tables, listings and figures) will be produced for each cohort (VPA and STP) using the following three treatment groups:

* GWP42003-P
* Placebo
* Overall

For each output, numbering will be the same for both cohorts, reference to the cohort will be indicated in the header (see below).

GW Pharmaceuticals - GWEP1447 DB Phase Analysis – VPA Cohort - Draft Version - - - - Confidential - - - -

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**All mockups**

**Section 12**

**Section 12.1 Demographic Data and Subject Characteristics**

1. Subject Disposition, Visit Attendance, Protocol Violations

1.1. Patients Screened by Country and Site

Screened Population

| Country    Site | Not randomized N=x Subjects  n % | Placebo  N=x Subjects  n % | GWP42003-P  N=xx Subjects  n % | All patients  N=xx Subjects  n % |
| --- | --- | --- | --- | --- |
|  | | | | |
| All countries | x (100.0) | x (100.0) | xx (100.0) | xx (100.0) |
|  | | | | |
| Romania | x (xx.x) | x ( xx.x) | x ( xx.x) | x ( xx.x) |
| 1261 |  | x ( xx.x) | x ( xx.x) | x ( xx.x) |
| 1289 | x (xx.x) |  | x ( xx.x) | x ( xx.x) |
|  | | | | |
| … |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
| Source: Listing 1.1 | | | | |
| Page x of x | | | | |

1. Subject Disposition, Visit Attendance, Protocol Violations

11-1. Patient Disposition

Screened Population

| Statistics | Not randomized  (N=x)   n (%) | Placebo  (N=x)   n (%) | GWP42003-P  (N=xx)   n (%) | Total  (N=xx)   n (%) |
| --- | --- | --- | --- | --- |
|  | | | | |
| Screened Subjects | x (100.0) | x (100.0) | xx (100.0) | xx (100.0) |
|  | | | | |
| Screen Failure | x (100.0) |  |  | x ( xx.x) |
| Withdrew Consent | x ( xx.x) |  |  | x ( xx.x) |
| … |  |  |  |  |
|  | | | | |
| Randomized |  | x (100.0) | xx (100.0) | xx ( xx.x) |
|  | | | | |
| Randomized and Treated Subjects |  | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  |  |  |  |  |
| Completed the DB Period |  | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Continued in OLE period |  |  |  |  |
| Continued to the Taper period |  | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Did not continue in OLE or Taper |  |  |  |  |
| Reason 1 |  |  |  |  |
| … |  |  |  |  |
| Did Not Complete the DB Period |  | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Patient/legal representative withdrew consent to participate |  | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| … |  | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Source: Listing 1.1 Percentages are generally based on the number of screened patients except for DB Period status for which percentages are based on randomized patients.  Page x of x | | | | |

Repeat this table on the safety and the PK populations.

1. Subject Disposition, Visit Attendance, Protocol Violations

11-2. Number of Patients by Visits

Screened Population

| Visit | Not randomized  (N=x)   n (%) | Placebo  (N=x)   n (%) | GWP42003-P  (N=xx)   n (%) | Total  (N=xx)   n (%) |
| --- | --- | --- | --- | --- |
|  | | | | |
| V1 (Day -14 to -7) | x ( xx.x) | x ( xx.x) | x ( xx.x) | x ( xx.x) |
|  | | | | |
| V2 (Day 1) |  | x ( xx.x) | x ( xx.x) | x ( xx.x) |
|  | | | | |
| V2 (Day 2) |  | x ( xx.x) | x ( xx.x) | x ( xx.x) |
|  | | | | |
| V3 (Day 12) |  | x ( xx.x) | x ( xx.x) | x ( xx.x) |
|  | | | | |
| V4 (Day 26) |  | x ( xx.x) | x ( xx.x) | x ( xx.x) |
|  | | | | |
| V4 (Day 27) |  | x ( xx.x) | x ( xx.x) | x ( xx.x) |
|  |  |  |  |  |
| … |  |  |  |  |
| Source: Listing 1.3  Page 1 of 1 | | | | |

2. Analysis Sets

2.1. Summary of Analysis Sets

Screened Population

| Population and reason for exclusion | Not randomized  (N=x)   n (%) | Placebo  (N=x)   n (%) | GWP42003-P  (N=xx)   n (%) | Total  (N=xx)   n (%) |
| --- | --- | --- | --- | --- |
|  | | | | |
| Screened | x (100.0) | x (100.0) | x (100.0) | x (100.0) |
| Withdrew Consent | x ( xx.x) |  |  | x ( xx.x) |
|  | | | | |
| Safety Population |  | x (100.0) | xx (100.0) | xx ( xx.x) |
|  | | | | |
| Pharmacokinetic Population\* |  | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Reason 1 |  | x ( xx.x) | x ( xx.x) | x ( xx.x) |
| Reason 2 |  |  | x ( xx.x) | x ( xx.x) |
| … |  |  | x ( xx.x) | x ( xx.x) |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
| Source: Listing 2 \* For the pharmacokinetic population, percentages are based on treated subjects.                                                                                                              Page 1 of 1 | | | | |

2. Analysis Sets

2.2. Summary of Anti-Epileptic Drugs

Safety Population

| Population    Anti-Epileptic Drug | Placebo  N=x Subjects  n % | GWP42003-P  N=xx Subjects  n % | All patients  N=xx Subjects  n % |
| --- | --- | --- | --- |
|  | | | |
| Safety Population | x | xx | xx |
| AE Drug 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| AE Drug 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... |  |  |  |
|  |  |  |  |
|  | | | |
| Pharmacokinetic Population | x | x | xx |
| AE Drug 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| AE Drug 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... |  |  |  |
|  |  |  |  |
| Source: Listing 6.2                                                                                      Page 1 of 1 | | | |

3. Demographics

3.1. Summary of Demographics

Safety Population

| Parameters | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- |
|  | | | | |
| Age (years) | N (missing) | x (x) | xx (xx) | xx (xx) |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  | | | | |
| Sex | N (missing) | x | xx | xx |
| Male | x ( xx.x) | x ( xx.x) | xx ( xx.x) |
| Female | x ( xx.x) | x ( xx.x) | xx ( xx.x) |
|  | | | | |
| Race | N (missing) | x | xx | xx |
| White/Caucasian | x (xx.x) | xx ( xx.x) | xx ( xx.x) |
| Black/African American | x (xx.x) | xx ( xx.x) | xx ( xx.x) |
| Asian | x (xx.x) | xx ( xx.x) | xx ( xx.x) |
| Native Hawaiian/Other Pacific Islander | x (xx.x) | xx ( xx.x) | xx ( xx.x) |
| Other | x (xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | | | | |
| Height (cm) | N (missing) | x (x) | xx (xx) | xx (xx) |
| Mean (SD) | xxx.xx (xx.xx) | xxx.xx (x.xx) | xxx.xx (xx.xx) |
| Median | xxx.xx | xxx.xx | xxx.xx |
| Q1 ; Q3 | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx |
| Min ; Max | xxx.x ; xxx.x | xxx.x ; xxx.x | xxx.x ; xxx.x |
|  | | | | |
| Weight (kg) | N (missing) | x (x) | xx (xx) | xx (xx) |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (x.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xxx.x | xx.x ; xxx.x | xx.x ; xxx.x |
| Source: Listing 3                                                                                           Page 1 of 2 | | | | |

3. Demographics

3.1. Summary of Demographics

Safety Population

| Parameters | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=XX) |
| --- | --- | --- | --- | --- |
|  | | | | |
| Body Mass Index (kg/m2) | n | x | xx | xx |
| Mean (SD) | xx.xx (x.xx) | xx.xx (xx.x) | xx.xx (xx.x) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
| Source: Listing 3                                                                                           Page 2 of 2 | | | | |

4. Baseline Disease Characteristics

4.1. Epilepsy Characteristics

Safety Population

| Parameters | Placebo  N=x Subjects  n % | GWP42003-P  N=xx Subjects  n % | All patients  N=xx Subjects  n % |
| --- | --- | --- | --- |
|  | | | |
| Ever Had Abnormal EEG? ->Yes | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | | | |
| Ever Had Abnormal Neuroimaging History? ->Yes | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | | | |
| Ever Had Genetic Testing? ->Yes | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | | | |
| History Of Current Seizures | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Absence or Atypical absence | x ( xx.x) | x ( xx.x) | x ( xx.x) |
| Atonic | x ( xx.x) | x ( xx.x) | x ( xx.x) |
| Complex Partial Seizure (Focal Dyscognitive) | x ( xx.x) | x ( xx.x) | x ( xx.x) |
| ... |  |  |  |
|  | | | |
| History Of Seizures No Longer Occurring | x ( xx.x) | x ( xx.x) | x ( xx.x) |
| Atonic | x ( xx.x) | x ( xx.x) | x ( xx.x) |
| Complex Partial Seizure (Focal Dyscognitive) | x ( xx.x) | x ( xx.x) | x ( xx.x) |
| ... |  |  |  |
|  |  |  |  |
| Source: Listing 4.1, 4.2, 4.3, 4.4, 4.5                                                                                               Page 1 of 1 | | | |

4. Baseline Disease Characteristics

4.2. Previous Use of Cannabis

Safety Population

| Parameters | Statistics | Placebo  (N=x)   n (%) | GWP42003-P  (N=xx)   n (%) | Total  (N=xx)   n (%) |
| --- | --- | --- | --- | --- |
|  | | | | |
| Has the patient previously used Cannabis? | n | x | xx | xx |
| Yes | x ( xx.x) | x ( xx.x) | x ( xx.x) |
| No | x ( xx.x) | x ( xx.x) | x ( xx.x) |
|  | | | | |
| Time since Last of use of Cannabis (Months) | n | x | x | x |
| Mean (SD) | xxx.x (xxx.x) | xxx.x (xxx.x) | xxx.x (xxx.x) |
| Median | xxx.x | xxx.x | xxx.x |
| Q1 ; Q3 | xxx.x ; xxx.x | xxx.x ; xxx.x | xxx.x ; xxx.x |
| Min ; Max | xxx ; xxx | xxx ; xxx | xxx ; xxx |
|  | | | | |
| Time since Last of use of Cannabis (Categorical) | n | x | xx | xx |
| ≤3 months | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | >3 months | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | | | | |
| Frequency of use of Cannabis | n | x | xx | xx |
| Missing | x ( xx.x) | x ( xx.x) | x ( xx.x) |
| Once per year | x ( xx.x) | x ( xx.x) | x ( xx.x) |
|  | Up to 12 times per year | x ( xx.x) | x ( xx.x) | x ( xx.x) |
|  | More than 12 times per year | x ( xx.x) | x ( xx.x) | x ( xx.x) |
| Source: Listing 4.6                                                                                                         Page 1 of 1 | | | | |

5. Non-Epilepsy Medical History

Safety Population

| System Organ Class    Preferred Term | Placebo  N=x Subjects  n % | GWP42003-P  N=xx Subjects  n % | All patients  N=xx Subjects  n % |
| --- | --- | --- | --- |
|  | | | |
| Subject with at least one non-epilepsy medical history | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | | | |
| SOC 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... |  |  |  |
|  | | | |
| SOC 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... |  |  |  |
|  | | | |
| ... |  |  |  |
|  |  |  |  |
| Source: Listing 5 If a subject has multiple histories within a system organ class or preferred term, the subject is counted once.                                                                                                      Page 1 of 1 | | | |

6. Medications

6.1. Medications Ongoing at Baseline

Safety Population

| ATC Level 2    Preferred Term | Placebo  N=x Subjects  n % | GWP42003-P  N=xx Subjects  n % | All patients  N=xx Subjects  n % |
| --- | --- | --- | --- |
|  | | | |
| Subject with at least one medication ongoing at baseline | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | | | |
| ATC 2 A | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... | | | |
|  | | | |
| ATC 2 B | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | | | |
| ... | | | |
|  | | | |
| ... |  |  |  |
| Source: Listing 6.3 Clobazam was taken by all patients as planned in the protocol and was excluded from the table. If a subject has multiple medications within an ATC level 2 or preferred term, the subject is counted once.                                                                                               Page 1 of 1 | | | |

6. Medications

6.2. Medications Concomitant to DB Treatment Period

Safety Population

| ATC Level 2    Preferred Term | Placebo  N=x Subjects  n % | GWP42003-P  N=xx Subjects  n % | All patients  N=xx Subjects  n % |
| --- | --- | --- | --- |
|  | | | |
| Subject with at least one medication concomitant to DB period | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | | | |
|  |  |  |  |
| ATC 2 A | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... |  |  |  |
|  |  |  |  |
| ATC 2 B | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 |  |  |  |
| ... |  |  |  |
|  |  |  |  |
| Source: Listing 6.3 Medications ongoing at baseline or started after baseline are included. Clobazam was taken by all patients as planned in the protocol and was excluded from the table. If a subject has multiple medications within an ATC level 2 or preferred term, the subject is counted once.                                                                                               Page 1 of 1 | | | |

7. Compliance

Safety Population

| Parameters | Statistics | Placebo  (N=x)   n (%) | GWP42003-P  (N=xx)   n (%) | Total  (N=xx)   n (%) |
| --- | --- | --- | --- | --- |
|  | | | | |
| Compliant? | n | x | xx | xx |
| No | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Yes | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Source: Listing 7 Compliant: The response to the question 'Did the patient comply with the dosing scheduled' is answered 'Yes' and, The response to the question 'Does the actual IMP usage reflect the expected amount used as per the dosing scheduled' is answered 'Yes' and, The response to the question 'Were there some signals of potential abuse since last visit' is answered 'No'. Not compliant: if the response to the 2 first questions above was 'No' at least once or the response to the third question is 'Yes' at least once. Unknown otherwise.                                                                                                   Page 1 of 1 | | | | |

**Section 12.2 Efficacy**

**Section 12.2.1 Pharmacokinetics**

8. Pharmacokinetics

8.1. PK Values

8.1.1. STP

PK Population

| Parameter | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Stiripentol (ng/mL) | D1-Pre-dose | n | x | xx | xx |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| Median | xxx.xx | xxx.xx | xxx.xx |
| Q1 ; Q3 | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx |
| Min ; Max | xxx.x ; xxx.x | xxx.x ; xxx.x | xxx.x ; xxx.x |
|  |  |  |  |
| n\* | x | xx | xx |
| G-Mean (CV%) | xxx.x (xx.x) | xxx.x (xx.x) | xxx.x (xx.x) |
|  | | | | | |
|  | D1-15 minutes post-dose | n | x | xx | xx |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| Median | xxx.xx | xxx.xx | xxx.xx |
| Q1 ; Q3 | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx |
| Min ; Max | xxx.x ; xxx.x | xxx.x ; xxx.x | xxx.x ; xxx.x |
|  |  |  |  |
| n\* | x | xx | xx |
| G-Mean (CV%) | xxx.x (xx.x) | xxx.x (xx.x) | xxx.x (xx.x) |
|  | … |  |  |  |  |
| Source: Listing 8.1 Geometric mean is derived for patients with concentration above LLOQ \* Number of patients with concentration above LLOQ 24 hour kinetic data points excluded from PK analysis and plasma concentration-time profiles (12 hour dosing interval).                                                                                                            Page 1 of X | | | | | |

**Programmer’s note:** All blood samples time points will be summarized (pre-dose, 15 minutes, 30 minutes, 1 hour, 1.5 hours, 2 hours, 4 hours, 6 hours, 12 hours, 24 hours post-dose) at Day 1 and Day 26.

This title is applicable for STP arm. For VPA arm that will be “8.1.1. VPA and Metabolites”, and VPA and 4-ene-VPA will be summarized at each timepoint for Day 1 and Day 26.

|  |  |
| --- | --- |
|  |  |

8. Pharmacokinetics

8.1. PK Values

8.1.2. CBD and Metabolites

PK Population

| Parameter | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Cannabidiol (ng/mL) | D26-Pre-dose | n | x | xx | xx |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| Median | xxx.xx | xxx.xx | xxx.xx |
| Q1 ; Q3 | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx |
| Min ; Max | xxx.x ; xxx.x | xxx.x ; xxx.x | xxx.x ; xxx.x |
|  |  |  |  |
| n\* | x | xx | xx |
| G-Mean (CV%) | xxx.x (xx.x) | xxx.x (xx.x) | xxx.x (xx.x) |
|  | | | | | |
|  | D26-15 minutes post-dose | n | x | xx | xx |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| Median | xxx.xx | xxx.xx | xxx.xx |
| Q1 ; Q3 | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx |
| Min ; Max | xxx.x ; xxx.x | xxx.x ; xxx.x | xxx.x ; xxx.x |
|  |  |  |  |
| n\* | x | xx | xx |
| G-Mean (CV%) | xxx.x (xx.x) | xxx.x (xx.x) | xxx.x (xx.x) |
|  | … |  |  |  |  |
|  |  |  |  |  |  |
| Source: Listing 8.1 Geometric mean is derived for patients with concentration above LLOQ \* Number of patients with concentration above LLOQ 24 hour kinetic data points excluded from PK analysis and plasma concentration-time profiles (12 hour dosing interval).                                                                                                            Page 1 of x | | | | | |

**Programmer’s note:** All blood samples time points will be summarized (pre-dose, 15 minutes, 30 minutes, 1 hour, 1.5 hours, 2 hours, 4 hours, 6 hours, 12 hours, 24 hours post-dose) at Day 26 for CBD and his metabolites (6-hydroxy cannabidiol, 7-carboxy cannabidiol, 7-hydroxy cannabidiol).

8. Pharmacokinetics

8.1. PK Values

8.1.3. THC and metabolites

PK Population

| Parameter | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Tetrahydrocannabinol (ng/mL) | D26-Pre-dose | n | x | xx | xx |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| Median | xxx.xx | xxx.xx | xxx.xx |
| Q1 ; Q3 | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx |
| Min ; Max | xxx.x ; xxx.x | xxx.x ; xxx.x | xxx.x ; xxx.x |
|  |  |  |  |
| n\* | x | xx | xx |
| G-Mean (CV%) | xxx.x (xx.x) | xxx.x (xx.x) | xxx.x (xx.x) |
|  | | | | | |
|  | D26-15 minutes post-dose | n | x | xx | xx |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| Median | xxx.xx | xxx.xx | xxx.xx |
| Q1 ; Q3 | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx |
| Min ; Max | xxx.x ; xxx.x | xxx.x ; xxx.x | xxx.x ; xxx.x |
|  |  |  |  |
| n\* | x | xx | xx |
| G-Mean (CV%) | xxx.x (xx.x) | xxx.x (xx.x) | xxx.x (xx.x) |
|  | … |  |  |  |  |
|  |  |  |  |  |  |
| Source: Listing 8.1 Geometric mean is derived for patients with concentration above LLOQ \* Number of patients with concentration above LLOQ 24 hour kinetic data points excluded from PK analysis and plasma concentration-time profiles (12 hour dosing interval).                                                                                                            Page 1 of x | | | | | |

**Programmer’s note:** All blood samples time points will be summarized (pre-dose, 15 minutes, 30 minutes, 1 hour, 1.5 hours, 2 hours, 4 hours, 6 hours, 12 hours, 24 hours post-dose) at Day 26 for THC and his metabolites (11-OH Tetrahydrocannabinol, 11-COOH Tetrahydrocannabinol).

8. Pharmacokinetics

8.1. PK Values

8.1.4. CLB and Metabolites

PK Population

| Parameter | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Clobazam (ng/mL) | D1-Pre-dose | n | x | xx | xx |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| Median | xxx.xx | xxx.xx | xxx.xx |
| Q1 ; Q3 | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx |
| Min ; Max | xxx.x ; xxx.x | xxx.x ; xxx.x | xxx.x ; xxx.x |
|  |  |  |  |
| n\* | x | xx | xx |
| G-Mean (CV%) | xxx.x (xx.x) | xxx.x (xx.x) | xxx.x (xx.x) |
|  | | | | | |
|  | D1-15 minutes post-dose | n | x | xx | xx |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| Median | xxx.xx | xxx.xx | xxx.xx |
| Q1 ; Q3 | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx |
| Min ; Max | xxx.x ; xxx.x | xxx.x ; xxx.x | xxx.x ; xxx.x |
|  |  |  |  |
| n\* | x | xx | xx |
| G-Mean (CV%) | xxx.x (xx.x) | xxx.x (xx.x) | xxx.x (xx.x) |
|  | … |  |  |  |  |
|  |  |  |  |  |  |
| Source: Listing 8.1 Geometric mean is derived for patients with concentration above LLOQ \* Number of patients with concentration above LLOQ 24 hour kinetic data points excluded from PK analysis and plasma concentration-time profiles (12 hour dosing interval).                                                                                                           Page 1 of x | | | | | |

**Programmer’s note:** All blood samples time points will be summarized (pre-dose, 15 minutes, 30 minutes, 1 hour, 1.5 hours, 2 hours, 4 hours, 6 hours, 12 hours, 24 hours post-dose) at Day 1 and Day 26 for CLB and his metabolite (N-Desmethylclobazam).

8. Pharmacokinetics

8.1. PK Values

8.1.5. Others AEDs

PK Population

| Parameter | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Levetiracetam (ng/mL) | D26-Pre-dose | n | x | xx | xx |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| Median | xxx.xx | xxx.xx | xxx.xx |
| Q1 ; Q3 | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx |
| Min ; Max | xxx.x ; xxx.x | xxx.x ; xxx.x | xxx.x ; xxx.x |
|  |  |  |  |
| n\* | x | xx | xx |
| G-Mean (CV%) | xxx.x (xx.x) | xxx.x (xx.x) | xxx.x (xx.x) |
|  | | | | | |
|  | D26-15 minutes post-dose | n | x | xx | xx |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| Median | xxx.xx | xxx.xx | xxx.xx |
| Q1 ; Q3 | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx | xxx.xx ; xxx.xx |
| Min ; Max | xxx.x ; xxx.x | xxx.x ; xxx.x | xxx.x ; xxx.x |
|  |  |  |  |
| n\* | x | xx | xx |
| G-Mean (CV%) | xxx.x (xx.x) | xxx.x (xx.x) | xxx.x (xx.x) |
|  | … |  |  |  |  |
|  |  |  |  |  |  |
| Source: Listing 8.1 For each drug, the subset of patients that took the drug is used. Geometric mean is derived for patients with concentration above LLOQ \* Number of patients with concentration above LLOQ 24 hour kinetic data points excluded from PK analysis and plasma concentration-time profiles (12 hour dosing interval).                                                                                                            Page 1 of x | | | | | |

**Programmer’s note:** All blood samples time points will be summarized (pre-dose, 15 minutes, 30 minutes, 1 hour, 1.5 hours, 2 hours, 4 hours, 6 hours, 12 hours, 24 hours post-dose) at Day 1 and Day 26 for levetiracetam (LEV) and topiramate (TPM).

8. Pharmacokinetics

8.1. PK Values

8.1.6. Summary

PK Population

|  |  | Placebo | | |  | | GWP42003-P | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Parameter | Visit | N | Mean(SD) | Median | |  | | N | Mean(SD) | Median |
|  | | | | | | | | | | |
| Stiripentol (ng/mL) | D1-Pre-dose | x | xxx.xx (xxx.xx) | (xxx.xx) | |  | | xx | xxx.xx (xxx.xx) | xxx.xx |
|  | D1-15 minutes post-dose | x | xxx.xx (xxx.xx) | (xxx.xx) | |  | | xx | xxx.xx (xxx.xx) | xxx.xx |
|  | D1-30 minutes post-dose | x | xxx.xx (xxx.xx) | (xxx.xx) | |  | | xx | xxx.xx (xxx.xx) | xxx.xx |
|  | … | x | xxx.xx (xxx.xx) | (xxx.xx) | |  | | xx | xxx.xx (xxx.xx) | xxx.xx |
|  |  |  |  |  | |  | |  |  |  |
| Cannabidiol (ng/mL) | D26-Pre-dose | x | xxx.xx (xxx.xx) | (xxx.xx) | |  | | xx | xxx.xx (xxx.xx) | xxx.xx |
|  | D26-15 minutes post-dose | x | xxx.xx (xxx.xx) | (xxx.xx) | |  | | xx | xxx.xx (xxx.xx) | xxx.xx |
|  | … |  |  |  | |  | |  |  |  |
| … |  |  |  |  | |  | |  |  |  |
|  |  |  |  |  | |  | |  |  |  |
| Source: Listing 8.1 24 hour kinetic data points excluded from PK analysis and plasma concentration-time profiles (12 hour dosing interval).                                                                                                              Page 1 of x | | | | | | | | | | |

**Programmer’s note:** All parameters and all blood samples time points from tables 8.1.1 to 8.1.5 will be summarized.

Stiripentol is applicable for STP arm. For VPA arm, VPA and 4-ene-VPA will be summarized.

8. Pharmacokinetics

8.2. PK Parameters

8.2.1. STP

PK Population

| Parameter | PK parameter | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | |
| Stiripentol | TMax (h) | Day 1 | n | x | xx | xx |
| Mean (SD) | x.xx (x.xx) | x.xx (x.xx) | x.xx (x.xx) |
| Median | x.xx | x.xx | x.xx |
| Q1 ; Q3 | x.xx ; x.xx | x.xx ; x.xx | x.xx ; x.xx |
| Min ; Max | x.x ; x.x | x.x ; x.x | x.x ; x.x |
|  |  |  |  |
| n\* | x | xx | xx |
| G-Mean (CV%) | x.x (xx.x) | x.x (xx.x) | x.x (xx.x) |
|  | | | | | | |
|  |  | Day 26 | n | x | xx | xx |
| Mean (SD) | x.xx (x.xx) | x.xx (x.xx) | x.xx (x.xx) |
| Median | x.xx | x.xx | x.xx |
| Q1 ; Q3 | x.xx ; x.xx | x.xx ; x.xx | x.xx ; x.xx |
| Min ; Max | x.x ; x.x | x.x ; x.x | x.x ; x.x |
|  |  |  |  |
| n\* | x | xx | xx |
| G-Mean (CV%) | x.x (xx.x) | x.x (xx.x) | x.x (xx.x) |
|  |  |  |  |  |  |  |
|  | Cmax (ng/mL) | … |  |  |  |  |
| Source: Listing 8.2 AUCtau and Cmax have been dose normalized by dividing the parameters by the dose expressed in mg/kg. \* Number of patients with parameter value above 0                                                                                                         Page 1 of x | | | | | | |

**Programmer’s note:** The following PK parameters: TMax, Cmax, Cmax normalized, AUCtau, AUCtau normalized, CLss/F and Vss/F will be summarized at Day 1 and Day 26.

This title is applicable for STP arm. For VPA arm that will be “8.2.1. VPA and Metabolites”, and the above PK parameters will be summarized for VPA and 4-ene-VPA at Day 1 and Day 26.

8. Pharmacokinetics

8.2. PK Parameters

8.2.2. CBD and Metabolites

PK Population

| Parameter | PK parameter | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | |
| Cannabidiol | TMax (h) | Day 26 | n | x | xx | xx |
| Mean (SD) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
| Median | xxx.xx | xxx.xx | xxx.xx |
| Q1 ; Q3 | xx.xx ; xxx.xx | xx.xx ; xxx.xx | xx.xx ; xxx.xx |
| Min ; Max | xx.x ; xxx.x | xx.x ; xxx.x | xx.x ; xxx.x |
|  |  |  |  |
| n\* | x | xx | xx |
| G-Mean (CV%) | xxx.x (xx.x) | xxx.x (xx.x) | xxx.x (xx.x) |
|  | … |  |  |  |  |  |
|  | | | | | | |
| Source: Listing 8.2 AUCtau and Cmax have been dose normalized by dividing the parameters by the dose expressed in mg/kg. \* Number of patients with parameter value above 0                                                                                                         Page 1 of x | | | | | | |

**Programmer’s note:** The following PK parameters: TMax, Cmax, Cmax normalized, AUCtau, AUCtau normalized, CLss/F and Vss/F will be summarized at Day 26 for CBD and his metabolites (6-hydroxy cannabidiol, 7-carboxy cannabidiol, 7-hydroxy cannabidiol).

8. Pharmacokinetics

8.2. PK Parameters

8.2.3. THC and Metabolites

PK Population

| Parameter | PK parameter | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | |
| Tetrahydrocannabinol | TMax (h) | Day 26 | n | x | xx | xx |
| Mean (SD) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
| Median | xxx.xx | xxx.xx | xxx.xx |
| Q1 ; Q3 | xx.xx ; xxx.xx | xx.xx ; xxx.xx | xx.xx ; xxx.xx |
| Min ; Max | xx.x ; xxx.x | xx.x ; xxx.x | xx.x ; xxx.x |
|  |  |  |  |
| n\* | x | xx | xx |
| G-Mean (CV%) | xxx.x (xx.x) | xxx.x (xx.x) | xxx.x (xx.x) |
|  | … |  |  |  |  |  |
|  | | | | | | |
| Source: Listing 8.2 AUCtau and Cmax have been dose normalized by dividing the parameters by the dose expressed in mg/kg. \* Number of patients with parameter value above 0                                                                                                         Page 1 of x | | | | | | |

**Programmer’s note:** The following PK parameters: TMax, Cmax, Cmax normalized, AUCtau, AUCtau normalized, CLss/F and Vss/F will be summarized at Day 26 for THC and his metabolites (11-OH Tetrahydrocannabinol, 11-COOH Tetrahydrocannabinol).

8. Pharmacokinetics

8.2. PK Parameters

8.2.4. CLB and Metabolites

PK Population

| Parameter | | PK parameter | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | |
| Clobazam | TMax (h) | | Day 1 | n | x | xx | xx |
| Mean (SD) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
| Median | xxx.xx | xxx.xx | xxx.xx |
| Q1 ; Q3 | xx.xx ; xxx.xx | xx.xx ; xxx.xx | xx.xx ; xxx.xx |
| Min ; Max | xx.x ; xxx.x | xx.x ; xxx.x | xx.x ; xxx.x |
|  |  |  |  |
| n\* | x | xx | xx |
| G-Mean (CV%) | xxx.x (xx.x) | xxx.x (xx.x) | xxx.x (xx.x) |
|  | … | |  |  |  |  |  |
|  |  | |  |  |  |  |  |
| Source: Listing 8.2 AUCtau and Cmax have been dose normalized by dividing the parameters by the dose expressed in mg/kg. \* Number of patients with parameter value above 0                                                                                                     Page 1 of x | | | | | | | |

**Programmer’s note:** The following PK parameters: TMax, Cmax, Cmax normalized, AUCtau, AUCtau normalized, CLss/F and Vss/F will be summarized at Day 1 and Day 26 for CLB and his metabolite (N-Desmethylclobazam).

8. Pharmacokinetics

8.2. PK Parameters

8.2.5. Other AEDs

PK Population

| Parameter | PK parameter | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | |
| Levetiracetam | TMax (h) | Day 1 | n | x | xx | xx |
| Mean (SD) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
| Median | xxx.xx | xxx.xx | xxx.xx |
| Q1 ; Q3 | xx.xx ; xxx.xx | xx.xx ; xxx.xx | xx.xx ; xxx.xx |
| Min ; Max | xx.x ; xxx.x | xx.x ; xxx.x | xx.x ; xxx.x |
|  |  |  |  |
| n\* | x | xx | xx |
| G-Mean (CV%) | xxx.x (xx.x) | xxx.x (xx.x) | xxx.x (xx.x) |
|  | … |  |  |  |  |  |
|  |  |  |  |  |  |  |
| Source: Listing 8.2 \* Number of patients with parameter value above 0                                                                                                             Page 1 of x | | | | | | |

**Programmer’s note:** The following PK parameters: TMax, Cmax, Cmax normalized, AUCtau, AUCtau normalized, CLss/F and Vss/F will be summarized at Day 1 and Day 26 for levetiracetam (LEV) and topiramate (TPM).

8. Pharmacokinetics

8.2. PK Parameters

8.2.6. Summary

PK Population

|  |  |  | Placebo | | | |  | | GWP42003-P | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Parameter | Summary | Visit | N | Mean(SD) | Median |  | | N | | Mean(SD) | Median |
|  | | | | | | | | | | | |
| Stiripentol | TMax (h) | D1 | x | xx.x (x.xx) | x.xx |  | | xx | | x.xx (x.xx) | x.xx |
| D26 | x | xx.x (x.xx) | x.xx |  | | xx | | x.xx (x.xx) | x.xx |
|  | | | | | | | | | | | |
|  | Cmax (ng/mL) | D1 | x | xx.xx (x.xx) | xx.xx |  | | xx | | xx.xx (x.xx) | xx.xx |
| D26 | x | xx.xx (x.xx) | xx.xx |  | | xx | | xx.xx (x.xx) | xx.xx |
|  |  |  |  |  |  |  | |  | |  |  |
|  | … |  |  |  |  |  | |  | |  |  |
|  |  |  |  |  |  |  | |  | |  |  |
| Cannabidiol | TMax (h) | D26 | x | xx.xx (x.xx) | xx.xx |  | | xx | | xx.xx (x.xx) | xx.xx |
| … |  |  |  |  |  |  | |  | |  |  |
|  |  |  |  |  |  |  | |  | |  |  |
| Source: Listing 8.2 For STP or VPA and Metabolites, AUCtau and Cmax have been dose normalized by dividing the parameters by the dose expressed in mg/kg. For each drug, the subset of patients that took the drug is used.                                                                                                            Page 1 of x | | | | | | | | | | | |

**Programmer’s note:** All parameters and PK parameters from tables 8.2.1 to 8.2.5 will be summarized at both visits Day 1 and Day 26 if applicable.

Stiripentol is applicable for STP arm. For VPA arm, VPA and 4-ene-VPA will be summarized.

8. Pharmacokinetics

8.3. Drug Drug Interaction

8.3.1. STP

PK Population

| Parameter | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Cmax (ng/mL) | Visit 2 Day 1 | n | x | x | x |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| G-Mean (CV%) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
|  | | | | | |
|  | Visit 4 Day 26 | n | x | x | x |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| G-Mean (CV%) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
|  | | | | | |
|  | Day 26 to Day 1 ratio | Ratio | x.xxx | x.xxx |  |
| 90%CI | [x.xxx – x.xxx] | [x.xxx – x.xxx] |  |
|  | | | | | |
| AUCtau (h\*ng/mL) | Visit 2 Day 1 | n | x | x | x |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| G-Mean (CV%) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
|  | | | | | |
|  | Visit 4 Day 26 | n | x | x | x |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| G-Mean (CV%) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
|  | | | | | |
|  | Day 26 to Day 1 ratio | Ratio | x.xxx | x.xxx |  |
| 90%CI | [x.xxx – x.xxx] | [x.xxx – x.xxx] |  |
| Source: Listing 8.2                                                                                                              Page 1 of 1 | | | | | |

**Programmer’s note:** This title is applicable for STP arm. For VPA arm that will be “8.3.1. VPA”, and the two above PK parameters will be summarized for VPA at Day 1 and Day 26, and the ratio as well.

8. Pharmacokinetics

8.3. Drug Drug Interaction

8.3.2. STP - Dose Normalized

PK Population

| Parameter | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Cmax (ng/mL) | Visit 2 Day 1 | n | x | x | x |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| G-Mean (CV%) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
|  | | | | | |
|  | Visit 4 Day 26 | n | x | x | x |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| G-Mean (CV%) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
|  | | | | | |
|  | Day 26 to Day 1 ratio | Ratio | x.xxx | x.xxx |  |
| 90%CI | [x.xxx – x.xxx] | [x.xxx – x.xxx] |  |
|  | | | | | |
| AUCtau (h\*ng/mL) | Visit 2 Day 1 | n | x | x | x |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| G-Mean (CV%) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
|  | | | | | |
|  | Visit 4 Day 26 | n | x | x | x |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| G-Mean (CV%) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
|  | | | | | |
|  | Day 26 to Day 1 ratio | Ratio | x.xxx | x.xxx |  |
| 90%CI | [x.xxx – x.xxx] | [x.xxx – x.xxx] |  |
| Source: Listing 8.2  AUCtau and Cmax have been dose normalized by dividing the parameters by the dose expressed in mg/kg.                                                                                                              Page 1 of 1 | | | | | |

**Programmer’s note:** This title is applicable for STP arm. For VPA arm that will be “8.3.2. VPA - Dose Normalized”, and the two above PK parameters will be summarized for VPA at Day 1 and Day 26, and the ratio as well.

8. Pharmacokinetics

8.3. Drug Drug Interaction

8.3.3. 4-ene-VPA

PK Population

| Parameter | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Cmax (ng/mL) | Visit 2 Day 1 | n | x | x | x |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| G-Mean (CV%) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
|  | | | | | |
|  | Visit 4 Day 26 | n | x | x | x |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| G-Mean (CV%) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
|  | | | | | |
|  | Day 26 to Day 1 ratio | Ratio | x.xxx | x.xxx |  |
| 90%CI | [x.xxx – x.xxx] | [x.xxx – x.xxx] |  |
|  | | | | | |
| AUCtau (h\*ng/mL) | Visit 2 Day 1 | n | x | x | x |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| G-Mean (CV%) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
|  | | | | | |
|  | Visit 4 Day 26 | n | x | x | x |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| G-Mean (CV%) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
|  | | | | | |
|  | Day 26 to Day 1 ratio | Ratio | x.xxx | x.xxx |  |
| 90%CI | [x.xxx – x.xxx] | [x.xxx – x.xxx] |  |
| Source: Listing 8.2                                                                                                              Page 1 of 1 | | | | | |

**Programmer’s note:** This table is only applicable for VPA arm.

8. Pharmacokinetics

8.3. Drug Drug Interaction

8.3.4. 4-ene-VPA - Dose Normalized

PK Population

| Parameter | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Cmax (ng/mL) | Visit 2 Day 1 | n | x | x | x |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| G-Mean (CV%) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
|  | | | | | |
|  | Visit 4 Day 26 | n | x | x | x |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| G-Mean (CV%) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
|  | | | | | |
|  | Day 26 to Day 1 ratio | Ratio | x.xxx | x.xxx |  |
| 90%CI | [x.xxx – x.xxx] | [x.xxx – x.xxx] |  |
|  | | | | | |
| AUCtau (h\*ng/mL) | Visit 2 Day 1 | n | x | x | x |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| G-Mean (CV%) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
|  | | | | | |
|  | Visit 4 Day 26 | n | x | x | x |
| Mean (SD) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) | xxx.xx (xxx.xx) |
| G-Mean (CV%) | xxx.xx (xx.xx) | xxx.xx (xx.xx) | xxx.xx (xx.xx) |
|  | | | | | |
|  | Day 26 to Day 1 ratio | Ratio | x.xxx | x.xxx |  |
| 90%CI | [x.xxx – x.xxx] | [x.xxx – x.xxx] |  |
| Source: Listing 8.2  AUCtau and Cmax have been dose normalized by dividing the parameters by the dose expressed in mg/kg.                                                                                                              Page 1 of 1 | | | | | |

**Programmer’s note:** This table is only applicable for VPA arm.

**Section 12.3 Safety**

**Section 12.3.1 Exposure to Study Medication**

10. Exposure

Safety Population

| Parameters | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- |
|  | | | | |
| Treatment Duration (Days) | n | x | xx | xx |
| Mean (SD) | xx.x (x.x) | xx.x (x.x) | xx.x (x.x) |
| Median | xx.x | xx.x | xx.x |
| Q1 ; Q3 | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
| Min ; Max | xx ; xx | xx ; xx | xx ; xx |
| Source: Listing 10.1                                                                                            Page 1 of 1 | | | | |

**Section 12.3.2 Adverse Events**

11. Adverse Events

11.1. Treatment-Emergent AEs

Safety Population

| System Organ Class    Preferred Term | Placebo  N=x Subjects  n % | GWP42003-P  N=xx Subjects  n % | All patients  N=xx Subjects  n % |
| --- | --- | --- | --- |
|  | | | |
| Subject with at least one treatment-emergent AE | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | | | |
| SOC 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... |  |  |  |
|  | | | |
| SOC 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... |  |  |  |
|  |  |  |  |
| ... |  |  |  |
|  |  |  |  |
| Source: Listing 11.1 If a subject has multiple events within a system organ class or preferred term, the subject is counted once. Events are sorted by decreased SOCs, PTs frequencies on the total column. In case of equal frequency, alphabetic order is used.                                                                                                         Page 1 of x | | | |

11. Adverse Events

11.2. Treatment-Emergent Related AEs

Safety Population

| System Organ Class    Preferred Term | Placebo  N=x Subjects  n % | GWP42003-P  N=xx Subjects  n % | All patients  N=xx Subjects  n % |
| --- | --- | --- | --- |
|  | | | |
| Subject with at least one treatment-emergent related AE | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | | | |
| SOC 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... |  |  |  |
|  |  |  |  |
| SOC 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... |  |  |  |
| ... |  |  |  |
| Source: Listing 11.1 If a subject has multiple events within a system organ class or preferred term, the subject is counted once. Events are sorted by decreased SOCs, PTs frequencies on the total column. In case of equal frequency, alphabetic order is used.                                                                                                         Page 1 of x | | | |

11. Adverse Events

11.3. Treatment-Emergent AEs by Maximum Severity

Safety Population

|  | Placebo N=x Subjects n % | | | |  | | GWP42003-P N=xx Subjects n % | | | |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| System Organ Class    Preferred Term | Mild | Moderate | Severe |  | | Mild | | Moderate | Severe |  | |
|  | | | | | | | | | | | |
| Subject with at least one treatment-emergent AE | x ( xx.x) | x ( xx.x) | x ( xx.x) |  | | x ( xx.x) | | x ( xx.x) | x ( xx.x) |  | |
|  | | | | | | | | | | | |
| SOC 1 | x ( xx.x) | x ( xx.x) | x ( xx.x) |  | | x ( xx.x) | | x ( xx.x) | x ( xx.x) |  | |
| PT 1 | x ( xx.x) | x ( xx.x) | x ( xx.x) |  | | x ( xx.x) | | x ( xx.x) | x ( xx.x) |  | |
| PT2 | x ( xx.x) | x ( xx.x) | x ( xx.x) |  | | x ( xx.x) | | x ( xx.x) | x ( xx.x) |  | |
| ... |  |  |  |  | |  | |  |  |  | |
|  | | | | | | | | | | | |
| SOC 2 | x ( xx.x) | x ( xx.x) | x ( xx.x) |  | | x ( xx.x) | | x ( xx.x) | x ( xx.x) |  | |
| PT 1 | x ( xx.x) | x ( xx.x) | x ( xx.x) |  | | x ( xx.x) | | x ( xx.x) | x ( xx.x) |  | |
| PT 2 | x ( xx.x) | x ( xx.x) | x ( xx.x) |  | | x ( xx.x) | | x ( xx.x) | x ( xx.x) |  | |
| ... |  |  |  |  | |  | |  |  |  | |
| ... |  |  |  |  | |  | |  |  |  | |
|  |  |  |  |  | |  | |  |  |  | |
| Source: Listing 11.1 For each SOC/PT, maximum severity is used. If a subject has multiple events within a system organ class or preferred term, the subject is counted once. Events are sorted by decreased SOCs, PTs frequencies on all subjects without taking into account the severity. In case of equal frequency, alphabetic order is used.                                                                                                              Page 1 of x | | | | | | | | | | | |

11. Adverse Events

11.4. Pre-Study AEs

Safety Population

| System Organ Class    Preferred Term | Placebo  N=x Subjects  n % | GWP42003-P  N=xx Subjects  n % | All patients  N=xx Subjects  n % |
| --- | --- | --- | --- |
|  | | | |
| Subject with at least one pre-study AE | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | | | |
| SOC 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... | | | |
|  |  |  |  |
| SOC 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | | | |
| ... |  |  |  |
| ... |  |  |  |
| Source: Listing 11.1 If a subject has multiple events within a system organ class or preferred term, the subject is counted once. Events are sorted by decreased SOCs, PTs frequencies on the total column. In case of equal frequency, alphabetic order is used.                                                                                                        Page 1 of x | | | |

**Section 12.3.3 Deaths, Other Serious And Significant Adverse Events**

12. Serious Adverse Events

12.1. SAEs

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Period | SOC/ PT/ Reported Term\* | Start Date (Day)/ End Date (Day)/ Duration | Serious Event | Severity/ Causality/ Outcome | Action Taken with Study Treatment |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | DB Period | Nervous system disorders / Seizure / Decompensated Epilepsy \* | 2016-09-28 (211)/ 2016-10-17 (230)/ 20 | Y | Severe/ Related / RECOVERED/RESOLVED | Drug Withdrawn |
|  | | | | | | | |
|  | GWEP1428-W-xxxx-xxx | OLE Period | Investigations / Alanine aminotransferase abnormal / Abnormal Alt Ast And Ggt Values \* | 2016-05-05 (92)/ 2016-06-16 (134)/ 43 | Y | Severe/ Related / RECOVERED/RESOLVED | Drug Withdrawn |
| … | | | | | | | |
|  | | | | | | | |
| \* Treatment-emergent SAE.                                                                                                                            Page 1 of 1 | | | | | | | |

12. Serious and Other Significant Adverse Events

12.1. Treatment-Emergent SAEs

Safety Population

| System Organ Class    Preferred Term | Placebo  N=x Subjects  n % | GWP42003-P  N=xx Subjects  n % | All patients  N=xx Subjects  n % |
| --- | --- | --- | --- |
|  | | | |
| Subject with at least one treatment-emergent SAE | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| SOC 1 |  |  |  |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... |  |  |  |
| SOC 1 |  |  |  |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... |  |  |  |
|  | | | |
| ... | | | |
|  | | | |
| Source: Listing 12.1 If a subject has multiple events within a system organ class or preferred term, the subject is counted once. Events are sorted by decreased SOCs, PTs frequencies on the total column. In case of equal frequency, alphabetic order is used.                                                                                               Page 1 of x | | | |

12. Serious and Other Significant Adverse Events

12.2. Treatment-Emergent Related SAEs

Safety Population

| System Organ Class    Preferred Term | Placebo  N=4 Subjects  n % | GWP42003-P  N=16 Subjects  n % | All patients  N=20 Subjects  n % |
| --- | --- | --- | --- |
|  | | | |
| Subject with at least one treatment-emergent related SAE | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| SOC 1 |  |  |  |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... |  |  |  |
| SOC 1 |  |  |  |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... |  |  |  |
|  |  |  |  |
| ... |  |  |  |
| Source: Listing 12.1 If a subject has multiple events within a system organ class or preferred term, the subject is counted once. Events are sorted by decreased SOCs, PTs frequencies on the total column. In case of equal frequency, alphabetic order is used.                                                                                               Page 1 of x | | | |

12. Serious and Other Significant Adverse Events

12.3. Treatment-Emergent AEs Reported as Leading to Permanent Cessation of Study Treatment

Safety Population

| System Organ Class    Preferred Term | Placebo  N=x Subjects  n % | GWP42003-P  N=xx Subjects  n % | All patients  N=xx Subjects  n % |
| --- | --- | --- | --- |
|  | | | |
| Subject with at least one treatment-emergent AE reported as leading to permanent cessation of study treatment | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| SOC 1 |  |  |  |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... | | | |
| SOC 1 |  |  |  |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... | | | |
|  |  |  |  |
| ... |  |  |  |
| Source: Listing 11.1 If a subject has multiple events within a system organ class or preferred term, the subject is counted once. Events are sorted by decreased SOCs, PTs frequencies on the total column. In case of equal frequency, alphabetic order is used.                                                                                                         Page 1 of 1 | | | |

12. Serious and Other Significant Adverse Events

12.4. Treatment-Emergent AEs Reported as Leading to Reduction of Study Treatment

Safety Population

| System Organ Class    Preferred Term | Placebo  N=x Subjects  n % | GWP42003-P  N=xx Subjects  n % | All patients  N=xx Subjects  n % |
| --- | --- | --- | --- |
|  | | | |
| Subject with at least one treatment-emergent AE reported as leading to reduction of study treatment | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| SOC 1 |  |  |  |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... | | | |
| SOC 1 |  |  |  |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... | | | |
|  |  |  |  |
| ... |  |  |  |
| Source: Listing 11.1 If a subject has multiple events within a system organ class or preferred term, the subject is counted once. Events are sorted by decreased SOCs, PTs frequencies on the total column. In case of equal frequency, alphabetic order is used.                                                                                                          Page 1 of x | | | |

12. Serious and Other Significant Adverse Events

12.5. All Fatal AEs

Safety Population

|  | | | |
| --- | --- | --- | --- |
| System Organ Class    Preferred Term | Placebo  N=x Subjects  n % | GWP42003-P  N=xx Subjects  n % | All patients  N=xx Subjects  n % |
|  |  |  |  |
| Subject with at least one treatment-emergent AE reported as Fatal | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| SOC 1 |  |  |  |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... |  |  |  |
| SOC 2 |  |  |  |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| ... |  |  |  |
|  |  |  |  |
| ... |  |  |  |
| Source: Listing 11.1 If a subject has multiple events within a system organ class or preferred term, the subject is counted once. Events are sorted by decreased SOCs, PTs frequencies on the total column. In case of equal frequency, alphabetic order is used.                                                                                                   Page 1 of x | | | |

12. Serious and Other Significant Adverse Events

12.6. Triggering Adverse Events

Safety Population

|  | | | | |
| --- | --- | --- | --- | --- |
| System Organ Class    Preferred Term | Placebo  N=x Subjects  n % | GWP42003-P  N=xx Subjects  n % | All patients  N=xx Subjects  n % |  |
|  |  |  |  |  |
| Subject with at least one treatment-emergent AE reported as triggering | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |  |
|  |  |  |  |  |
| SOC 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |  |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |  |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |  |
| ... |  |  |  |  |
| SOC 2 |  |  |  |  |
| PT 1 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |  |
| PT 2 | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |  |
| ... |  |  |  |  |
| ... |  |  |  |  |
| Source: Listing 11.1 Triggering events of interest are defined in the statistical analysis plan in section 4.8. If a subject has multiple events within a system organ class or preferred term, the subject is counted once. Events are sorted by decreased SOCs, PTs frequencies on the total column. In case of equal frequency, alphabetic order is used.                                                                                                      Page 1 of x | | | | |

**Section 12.3.4 Laboratory Data**

13. Laboratory Evaluations

13.1. Biochemistry

13.1.1. Value by Visit

Safety Population

| Parameter (Unit) | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Alanine aminotransferase (U/L) | V1 (Day -14 to -7) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  | | | | | |
|  | V2 (Day 1) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  | | | | | |
|  | Baseline | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  | | | | | |
|  | V3 (Day 12) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
| Source: Listing 13.1 Baseline is defined as the last available measurements obtained during the screening period, prior to first IMP dose administration.                                                                                                         Page 1 of x | | | | | |

13. Laboratory Evaluations

13.1. Biochemistry

13.1.1. Value by Visit

Safety Population

| Parameter (Unit) | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Alanine aminotransferase (U/L) | V4 (Day 26) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  | | | | | |
| Albumin (g/L) | V1 (Day -14 to -7) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
| … | | | | | |
|  | | | | | |
| Source: Listing 13.1 Baseline is defined as the last available measurements obtained during the screening period, prior to first IMP dose administration.                                                                                                         Page 2 of x | | | | | |

**Programmer’s note:** All biochemistry parameters will be summarized in this table. Visits according to the studied period will be summarized. For DB period, visits up to V4 (Day 26) will be included; for OLE period, visits from V5 (Week 2) will be included.

13. Laboratory Evaluations

13.1. Biochemistry

13.1.2. Change from Baseline by Visit

Safety Population

| Parameter (Unit) | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Alanine aminotransferase (U/L) | V3 (Day 12) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  | | | | | |
|  | V4 (Day 26) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
| … |  |  |  |  |  |
|  | | | | | |
| Source: Listing 13.1 Baseline is defined as the last available measurements obtained during the screening period, prior to first IMP dose administration.                                                                                                         Page 1 of x | | | | | |

**Programmer’s note:** All biochemistry parameters will be summarized in this table. Visits according to the studied period will be summarized. Only post-baseline visits will be displayed. For DB period, visits up to V4 (Day 26) will be included; for OLE period, visits from V5 (Week 2) will be included.

13. Laboratory Evaluations

13.1. Biochemistry

13.1.3. Shift from Baseline Based on Reference Ranges

Safety Population

| Parameter (Unit) | Visit | Statistics | Placebo  (N=x)   n (%) | GWP42003-P  (N=xx)   n (%) | Total  (N=xx)   n (%) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Alanine aminotransferase (U/L) | V3 (Day 12) | n | x | xx | xx |
| Low to Low | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Low to Normal | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Low to High | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Normal to Low | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Normal to Normal | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Normal to High | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| High to Low | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| High to Normal | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| High to High | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | | | | | |
|  | V4 (Day 26) | n | x | xx | xx |
|  |  | Low to Low | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  |  | Low to Normal | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  |  | … |  |  |  |
|  |  |  |  |  |  |
| … |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
| Source: Listing 13.1 Baseline is defined as the last available measurements obtained during the screening period, prior to first IMP dose administration.                                                                                                         Page 1 of x | | | | | |

**Programmer’s note:** All biochemistry parameters with available normal range indicators will be summarized in this table. Visits according to the studied period will be summarized. Only post-baseline visits will be displayed. For DB period, visits up to V4 (Day 26) will be included; for OLE period, visits from V5 (Week 2) will be included.

13. Laboratory Evaluations

13.1. Biochemistry

13.1.4. Shift from Baseline Based on Toxicity Limits

Safety Population

| Parameter (Unit) | Visit | Statistics | Placebo  (N=x)   n (%) | GWP42003-P  (N=xx)   n (%) | Total  (N=xx)   n (%) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Alanine aminotransferase (U/L) | V3 (Day 12) | n | x | xx | xx |
| No tox to No tox | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  |  | No tox to Tox increased | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  |  | … |  |  |  |
|  | | | | | |
|  | V4 (Day 26) | n | x | xx | xx |
| No tox to No tox | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  |  | … |  |  |  |
| … |  |  |  |  |  |
|  |  |  |  |  |  |
| Source: Listing 13.1 Baseline is defined as the last available measurements obtained during the screening period, prior to first IMP dose administration.                                                                                                            Page 1 of x | | | | | |

**Programmer’s note:** All biochemistry parameters included in Table 4 in the SAP will be summarized in this table. Visits according to the studied period will be summarized. Only post-baseline visits will be displayed. For DB period, visits up to V4 (Day 26) will be included; for OLE period, visits from V5 (Week 2) will be included.

13. Laboratory Evaluations

13.2. Hematology

13.2.1. Value by Visit

Safety Population

| Parameter (Unit) | | Visit | | | Statistics | | Placebo  (N=4) | | GWP42003-P  (N=16) | | Total  (N=20) |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | | | | |
| Absolute basophil count (10/L) | | V1 (Day -14 to -7) | | | n | | x | | xx | | xx |
| Mean (SD) | | xx.xx (xx.xx) | | xx.xx (xx.xx) | | xx.xx (xx.xx) |
| Median | | xx.xx | | xx.xx | | xx.xx |
| Q1 ; Q3 | | xx.xx ; xx.xx | | xx.xx ; xx.xx | | xx.xx ; xx.xx |
| Min ; Max | | xx.x ; xx.x | | xx.x ; xx.x | | xx.x ; xx.x |
|  | | | | | | | | | | | |
|  | | V2 (Day 1) | | | n | | x | | xx | | xx |
| Mean (SD) | | xx.xx (xx.xx) | | xx.xx (xx.xx) | | xx.xx (xx.xx) |
| Median | | xx.xx | | xx.xx | | xx.xx |
| Q1 ; Q3 | | xx.xx ; xx.xx | | xx.xx ; xx.xx | | xx.xx ; xx.xx |
| Min ; Max | | xx.x ; xx.x | | xx.x ; xx.x | | xx.x ; xx.x |
|  | | | | | | | | | | | |
|  | | Baseline | | | n | | xx.xx (xx.xx) | | xx.xx (xx.xx) | | xx.xx (xx.xx) |
| Mean (SD) | | xx.xx | | xx.xx | | xx.xx |
| Median | | xx.xx ; xx.xx | | xx.xx ; xx.xx | | xx.xx ; xx.xx |
| Q1 ; Q3 | | xx.x ; xx.x | | xx.x ; xx.x | | xx.x ; xx.x |
| Min ; Max | | x | | xx | | xx |
|  | | | | | | | | | | | |
| … |  | |  |  | |  | |  | |  | |
|  |  | |  |  | |  | |  | |  | |
| Source: Listing 13.1 Baseline is defined as the last available measurements obtained during the screening period, prior to first IMP dose administration.                                                                                                         Page 1 of x | | | | | | | | | | | |

**Programmer’s note:** All hematology parameters will be summarized in this table. Visits according to the studied period will be summarized. For DB period, visits up to V4 (Day 26) will be included; for OLE period, visits from V5 (Week 2) will be included.

13. Laboratory Evaluations

13.2. Hematology

13.2.2. Change from Baseline by Visit

Safety Population

| Parameter (Unit) | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Absolute basophil count (10/L) | V3 (Day 12) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  | | | | | |
|  | V4 (Day 26) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
| … |  |  |  |  |  |
|  | | | | | |
| Source: Listing 13.1 Baseline is defined as the last available measurements obtained during the screening period, prior to first IMP dose administration.                                                                                                         Page 1 of x | | | | | |

**Programmer’s note:** All hematology parameters will be summarized in this table. Visits according to the studied period will be summarized. Only post-baseline visits will be displayed. For DB period, visits up to V4 (Day 26) will be included; for OLE period, visits from V5 (Week 2) will be included.

13. Laboratory Evaluations

13.2. Hematology

13.2.3. Shift from Baseline Based on Reference Ranges

Safety Population

| Parameter (Unit) | Visit | Statistics | Placebo  (N=x)   n (%) | GWP42003-P  (N=xx)   n (%) | Total  (N=xx)   n (%) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Absolute basophil count (10/L) | V3 (Day 12) | n | x | xx | xx |
| Low to Low | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Low to Normal | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Low to High | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Normal to Low | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Normal to Normal | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Normal to High | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| High to Low | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| High to Normal | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| High to High | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | | | | | |
|  | V4 (Day 26) | n | x | xx | xx |
| Low to Low | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  |  | … |  |  |  |
| … |  |  |  |  |  |
|  | | | | | |
| Source: Listing 13.1 Baseline is defined as the last available measurements obtained during the screening period, prior to first IMP dose administration.                                                                                                         Page 1 of … | | | | | |

**Programmer’s note:** All hematology parameters with available normal range indicators will be summarized in this table. Visits according to the studied period will be summarized. Only post-baseline visits will be displayed. For DB period, visits up to V4 (Day 26) will be included; for OLE period, visits from V5 (Week 2) will be included.

13. Laboratory Evaluations

13.2. Hematology

13.2.4. Shift from Baseline Based on Toxicity Limits

Safety Population

| Parameter (Unit) | Visit | Statistics | Placebo  (N=x)   n (%) | GWP42003-P  (N=xx)   n (%) | Total  (N=xx)   n (%) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Absolute basophil count (10/L) | V3 (Day 12) | n | x | xx | xx |
| No tox to No tox | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  |  | No tox to Tox increased | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  |  | … |  |  |  |
|  | | | | | |
|  | V4 (Day 26) | n | x | xx | xx |
| No tox to No tox | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  |  | … |  |  |  |
|  | | | | | |
| Source: Listing 13.1 Baseline is defined as the last available measurements obtained during the screening period, prior to first IMP dose administration.                                                                                                            Page 1 of x | | | | | |

**Programmer’s note:** All hematology parameters included in Table 5 in the SAP will be summarized in this table. Visits according to the studied period will be summarized. Only post-baseline visits will be displayed. For DB period, visits up to V4 (Day 26) will be included; for OLE period, visits from V5 (Week 2) will be included.

13. Laboratory Evaluations

13.3. Urinalysis

13.3.1. Value by Visit

Safety Population

| Parameter (Unit) | | Visit | Statistics | Placebo  (N=x) | GWP42003-P  (N=xx) | Total  (N=xx) |
| --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | |
| Epithelial renal (/hpf) | | V1 (Day -14 to -7) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  | | | | | | |
|  | | V2 (Day 1) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  | | | | | | |
|  | | Baseline | n | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Mean (SD) | xx.xx | xx.xx | xx.xx |
| Median | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Q1 ; Q3 | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
| Min ; Max | x | xx | xx |
| … | | | | | | |
|  |  | |  |  |  |  |
| Source: Listing 13.1 Baseline is defined as the last available measurements obtained during the screening period, prior to first IMP dose administration.                                                                                                         Page 1 of x | | | | | | |

**Programmer’s note:** All urinalysis parameters will be summarized in this table. Visits according to the studied period will be summarized. For DB period, visits up to V4 (Day 26) will be included; for OLE period, visits from V5 (Week 2) will be included.

13. Laboratory Evaluations

13.3. Urinalysis

13.3.2. Change from Baseline by Visit

Safety Population

| Parameter (Unit) | Visit | Statistics | Placebo (N=x) | GWP42003-P (N=xx) | Total (N=xx) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Epithelial renal (/hpf) | V3 (Day 12) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  | | | | | |
|  | V4 (Day 26) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
| … |  |  |  |  |  |
|  | | | | | |
| Source: Listing 13.1 Baseline is defined as the last available measurements obtained during the screening period, prior to first IMP dose administration.                                                                                                        Page 1 of x | | | | | |

**Programmer’s note:** All urinalysis parameters will be summarized in this table. Visits according to the studied period will be summarized. Only post-baseline visits will be displayed. For DB period, visits up to V4 (Day 26) will be included; for OLE period, visits from V5 (Week 2) will be included.

13. Laboratory Evaluations

13.3. Urinalysis

13.3.3. Shift from Baseline Based on Reference Ranges

Safety Population

| Parameter (Unit) | Visit | Statistics | Placebo (N=4) | GWP42003-P (N=16) | Total (N=20) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Epithelial renal (/hpf) | V3 (Day 12) | n | x | xx | xx |
| Normal to Normal | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  |  | … |  |  |  |
|  | | | | | |
|  | V4 (Day 26) | n | x | xx | xx |
| Normal to Normal | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  |  | … |  |  |  |
| … |  |  |  |  |  |
|  |  |  |  |  |  |
| Source: Listing 13.1 Baseline is defined as the last available measurements obtained during the screening period, prior to first IMP dose administration.                                                                                                        Page 1 of x | | | | | |

**Programmer’s note:** All urinalysis parameters with available normal range indicators will be summarized in this table. Visits according to the studied period will be summarized. Only post-baseline visits will be displayed. For DB period, visits up to V4 (Day 26) will be included; for OLE period, visits from V5 (Week 2) will be included.

**Section 12.3.5 Listings of Abnormal Laboratory Values**

13. Laboratory Evaluations

13.2. Patients/Parameters with Abnormalities (Values Outside Reference or Toxicity Limits)

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Category/ Parameter | Analysis Visit | Date and Time (Day) Assessment | Analysis Value | Change/ % Change from Baseline | Indicator (RR) | Toxicity Grade |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | Biochemistry/ Alanine aminotransferase (U/L) | Visit x | yyyymmdd:hh:mm (xx) | xxx | xxx/xxx.xx | H [xx-xx] | Tox increased |
|  | | | | | | | | |
|  |  | Biochemistry/ Alkaline phosphatase (U/L) | Visit x | yyyymmdd:hh:mm (xx) | xxx | xxx/xxx.xx | L [xx-xx] |  |
|  | | | | | | | | |
|  |  | … |  |  |  |  |  |  |
|  | | | | | | | | |
|  |  |  |  |  |  |  |  |  |
| Page 1 of x | | | | | | | | |

**Section 12.3.6 Vital Signs, Other Physical Findings and Other Safety Data**

14. Vital signs, Other Physical Findings and Other Observations Related to Safety

14.1. Vital Signs

14.1.1. Value by Visit

Safety Population

| Parameter (Unit) | Visit | Statistics | Placebo  (N=4)   n (%) | GWP42003-P  (N=16)   n (%) | Total  (N=20)   n (%) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| VS/BP/PE indicative of medical condition? | Anytime post baseline | n | x | xx | xx |
| Yes | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| No | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | | | | | |
| Weight (kg) | V1 (Day -14 to -7) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  | | | | | |
|  | V2 (Day 1) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
| … | | | | | |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
| Source: Listing 14.1 VS=Vital Signs; BP=Blood Pressure; PE=Physical Examination. Baseline is defined as the last available measurements obtained during the screening period, prior to first IMP dose administration.                                                                                                         Page 1 of x | | | | | |

**Programmer’s note:** Weight, DBP, SBP, pulse rate, temperature and respiratory rate will be summarized in this table. Visits according to the studied period will be summarized. For DB period, visits up to V4 (Day 27) including baseline will be included; for OLE period, visits from V5 (Week 2) will be included.

14. Vital signs, Other Physical Findings and Other Observations Related to Safety

14.1. Vital Signs

14.1.2. Change from Baseline by Visit

Safety Population

| Parameter (Unit) | Visit | Statistics | Placebo  (N=4) | GWP42003-P  (N=16) | Total  (N=20) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Weight (kg) | V2 (Day 2) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  | | | | | |
|  | V3 (Day 12) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
| … |  |  |  |  |  |
|  | | | | | |
| Source: Listing 14.1 Baseline is defined as the last available measurements obtained during the screening period, prior to first IMP dose administration.                                                                                                         Page 1 of … | | | | | |

**Programmer’s note:** Weight, DBP, SBP, pulse rate, temperature and respiratory rate will be summarized in this table. Visits according to the studied period will be summarized. Only post-baseline visits will be displayed. For DB period, visits up to V4 (Day 27) including baseline will be included; for OLE period, visits from V5 (Week 2) will be included.

14. Vital signs, Other Physical Findings and Other Observations Related to Safety

14.2. ECG

14.2.1. Value by Visit

Safety Population

| Parameter (Unit) | Visit | Statistics | Placebo  (N=x)   n (%) | GWP42003-P  (N=xx)   n (%) | Total  (N=xx)   n (%) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| ECG indicative of medical condition? | Anytime post baseline | n | x | xx | xx |
| Yes | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| No | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | | | | | |
| PR Interval (msec) | V1 (Day -14 to -7) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  | | | | | |
|  | V2 (Day 1) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
| … |  |  |  |  |  |
|  | | | | | |
| Source: Listing 14.2 Baseline is defined as the last available measurements obtained during the screening period, prior to first IMP dose administration.                                                                                                              Page 1 of x | | | | | |

**Programmer’s note:** PR interval, QRS duration, QT interval, QTcB, ventricular rate, rythm, ST or T-wave changes and Infarct pattern/R-wave progression will be summarized in this table. Visits according to the studied period will be summarized. For DB period, visits up to V4 (Day 26) including baseline will be included; for OLE period, visits from V5 (Week 2) will be included.

14. Vital signs, Other Physical Findings and Other Observations Related to Safety

14.2. ECG

14.2.2 Change from Baseline by Visit

Safety Population

| Parameter (Unit) | Visit | Statistics | Placebo  (N=x)   n (%) | GWP42003-P  (N=xx)   n (%) | Total  (N=xx)   n (%) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| PR Interval (msec) | V3 (Day 12) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  | | | | | |
|  | V4 (Day 26) | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
| … |  |  |  |  |  |
|  |  |  |  |  |  |
| Source: Listing 14.2 Baseline is defined as the last available measurements obtained during the screening period, prior to first IMP dose administration.                                                                                                              Page 1 of x | | | | | |

**Programmer’s note:** PR interval, QRS duration, QT interval, QTcB, ventricular rate, rythm, ST or T-wave changes and Infarct pattern/R-wave progression will be summarized in this table. Only post-baseline visits will be displayed. Visits according to the studied period will be summarized. For DB period, visits up to V4 (Day 26) including baseline will be included; for OLE period, visits from V5 (Week 2) will be included.

14. Vital signs, Other Physical Findings and Other Observations Related to Safety

14.3. C-SSRS

Safety Population

| Parameter | Period | Statistics | Placebo  (N=4)   n (%) | GWP42003-P  (N=16)   n (%) | Total  (N=20)   n (%) |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| Wish to be dead | Baseline | n | x | xx | xx |
| Yes | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| No | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | | | | | |
|  | DB period | n | x | xx | xx |
| Yes | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| No | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | | | | | |
| Non-Specific Active Suicidal Thoughts | Baseline | n | x | xx | xx |
| Yes | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| No | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
|  | | | | | |
|  | DB period | n | x | xx | xx |
| Yes | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| No | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| … | | | | | |
|  | | | | | |
| Source: Listing 14.4                                                                                                              Page 1 of x | | | | | |

**Programmer’s note:** All C-SSRS categories including the ones derived in the SAP will be summarized in this table. Baseline, DB and OLE periods will be summarized. For baseline, visits up to V2 (Day 1) will be including; for DB period, visits up to V4 (Day 26) will be included; for OLE period, visits from V5 (Week 2) will be included.

14. Vital signs, Other Physical Findings and Other Observations Related to Safety

14.4. Seizure data

14.4.1. Average Daily Seizures - Descriptive Statistics

Safety Population

| Period | Statistics | Placebo  (N=4) | GWP42003-P  (N=16) | Total  (N=20) |
| --- | --- | --- | --- | --- |
|  | | | | |
| Screening | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  | | | | |
| DB Period | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  | | | | |
| OLE Period | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  |  |  |  |  |
| Source: Listing 14.5 Average daily seizures is derived, within patients, as the number of seizures divided by the number of days with evaluation.                                                                                Page 1 of 1 | | | | |

**Programmer’s note:** For DB period, visits up to V4 (Day 26) will be included; for OLE period, visits from V5 (Week 2) will be included.

14. Vital signs, Other Physical Findings and Other Observations Related to Safety

14.4. Seizure data

14.4.2. Average Daily Seizures - Change from Baseline

Safety Population

| Parameters | Statistics | Placebo  (N=4) | GWP42003-P  (N=16) | Total  (N=20) |
| --- | --- | --- | --- | --- |
|  | | | | |
| Change from Baseline | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  | | | | |
| Percent Change from Baseline | n | x | xx | xx |
| Mean (SD) | xx.xx (xx.xx) | xx.xx (xx.xx) | xx.xx (xx.xx) |
| Median | xx.xx | xx.xx | xx.xx |
| Q1 ; Q3 | xx.xx ; xx.xx | xx.xx ; xx.xx | xx.xx ; xx.xx |
| Min ; Max | xx.x ; xx.x | xx.x ; xx.x | xx.x ; xx.x |
|  | | | | |
| % Improvement | n | x | xx | xx |
| >25% worsening | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| -25 to 25%, no change | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| 25-50% improvement | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| 50-75% improvement | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| >75% improvement | x ( xx.x) | xx ( xx.x) | xx ( xx.x) |
| Source: Listing 14.5 Negative changes represent a decrease in seizures and thus an improvement. Baseline is defined as the last available measurements obtained during the screening period, prior to first IMP dose administration.                                                                                               Page 1 of 1 | | | | |

**Programmer’s note:** Table will be produced at DB and OLE analysis.

For DB period, visits up to V4 (Day 26) will be included; for OLE period, visits from V5 (Week 2) will be included.

**Section 12.4 Figures**

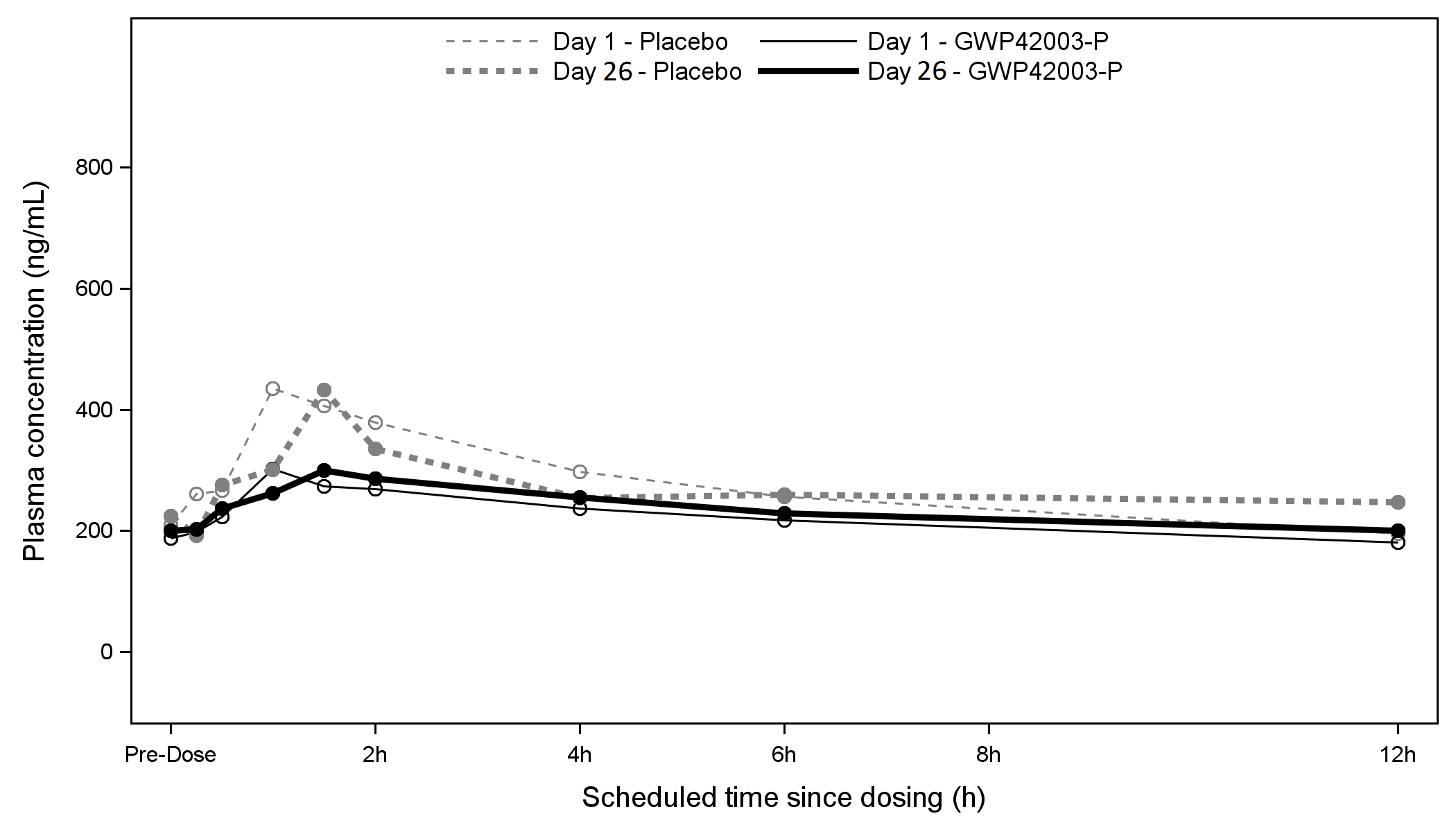
**Programmer’s note:** For all plasma concentration (8.1, 8.2 and 8.3) figures, 24h post-dose time point won’t be included.

8. Pharmacokinetics

8.1. PK Mean Profile

8.1.1a. Stiripentol - Geometric Means

PK Population



Source: Table 8.1.5

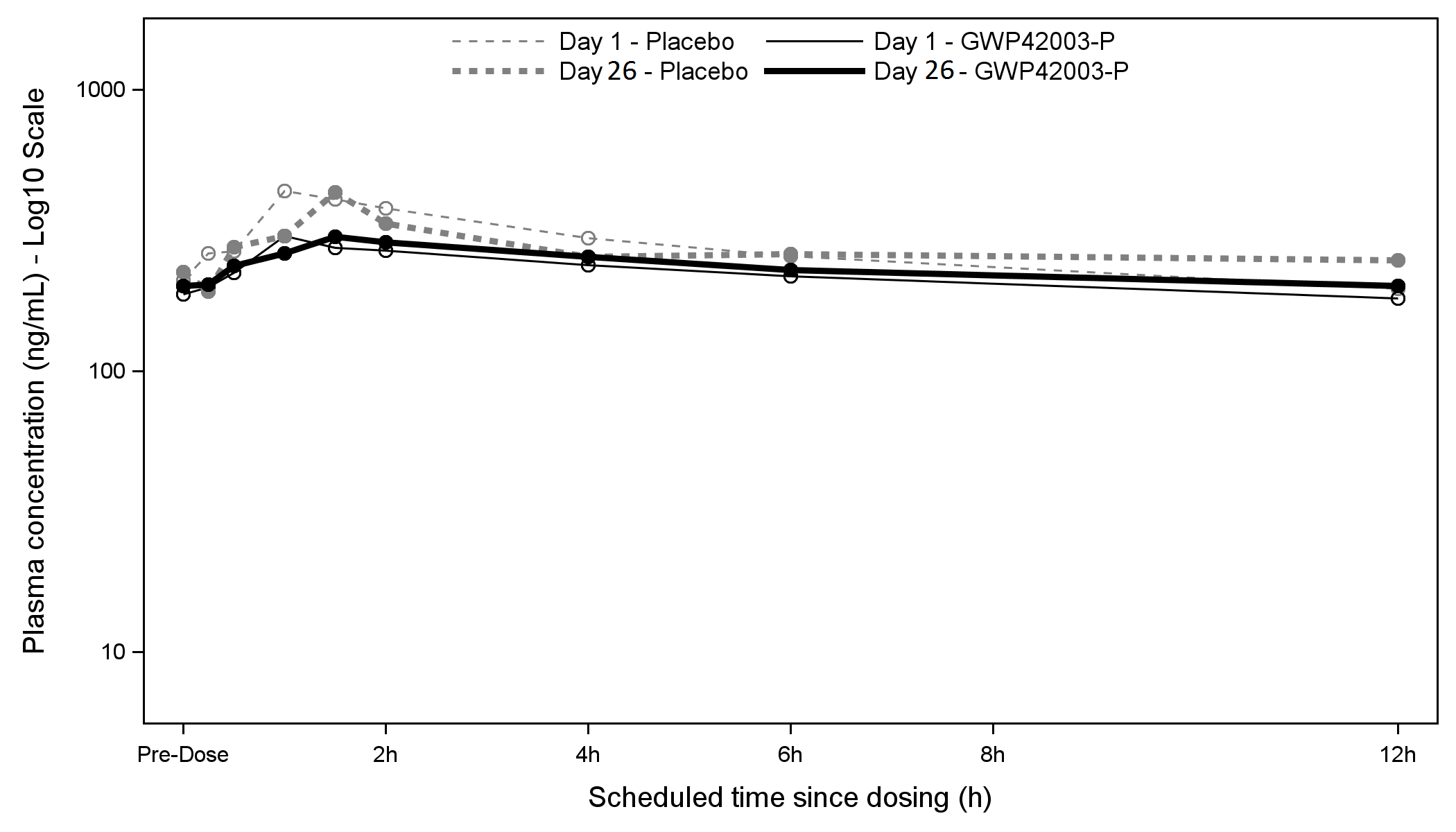
**Programmer’s note:** This title is applicable for STP arm. For VPA arm that will be “8.1.1a. Valproic Acid - Geometric Means”.

8. Pharmacokinetics

8.1. PK Mean Profile

8.1.1b. Stiripentol - Geometric Means - Log10 Scale

PK Population



Source: Table 8.1.5

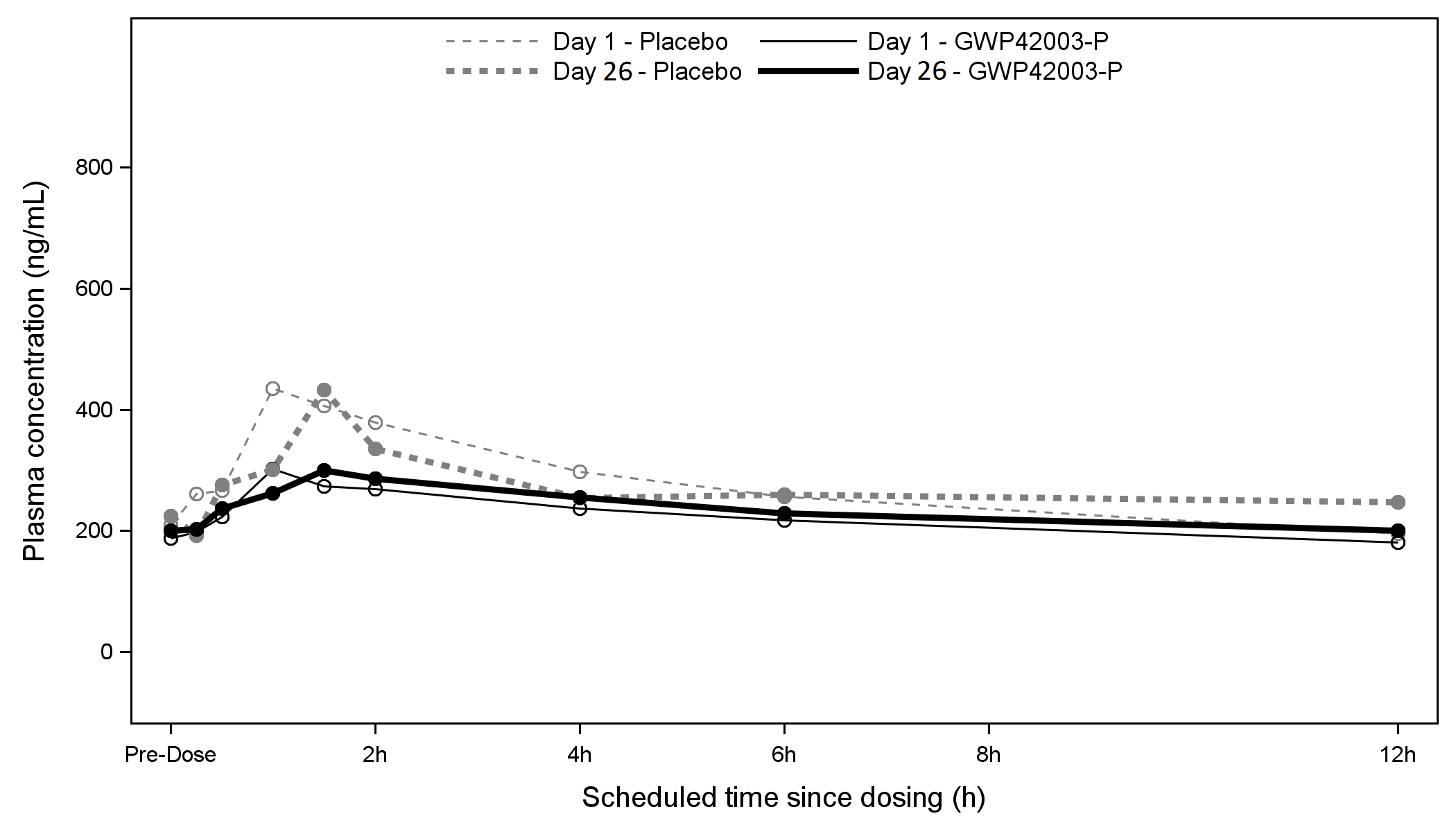
**Programmer’s note:** This title is applicable for STP arm. For VPA arm that will be “8.1.1b. Valproic Acid - Geometric Means - Log10 Scale”.

8. Pharmacokinetics

8.1. PK Mean Profile

8.1.2a. 4-ene-VPA - Geometric Means

PK Population



Source: Table 8.1.5

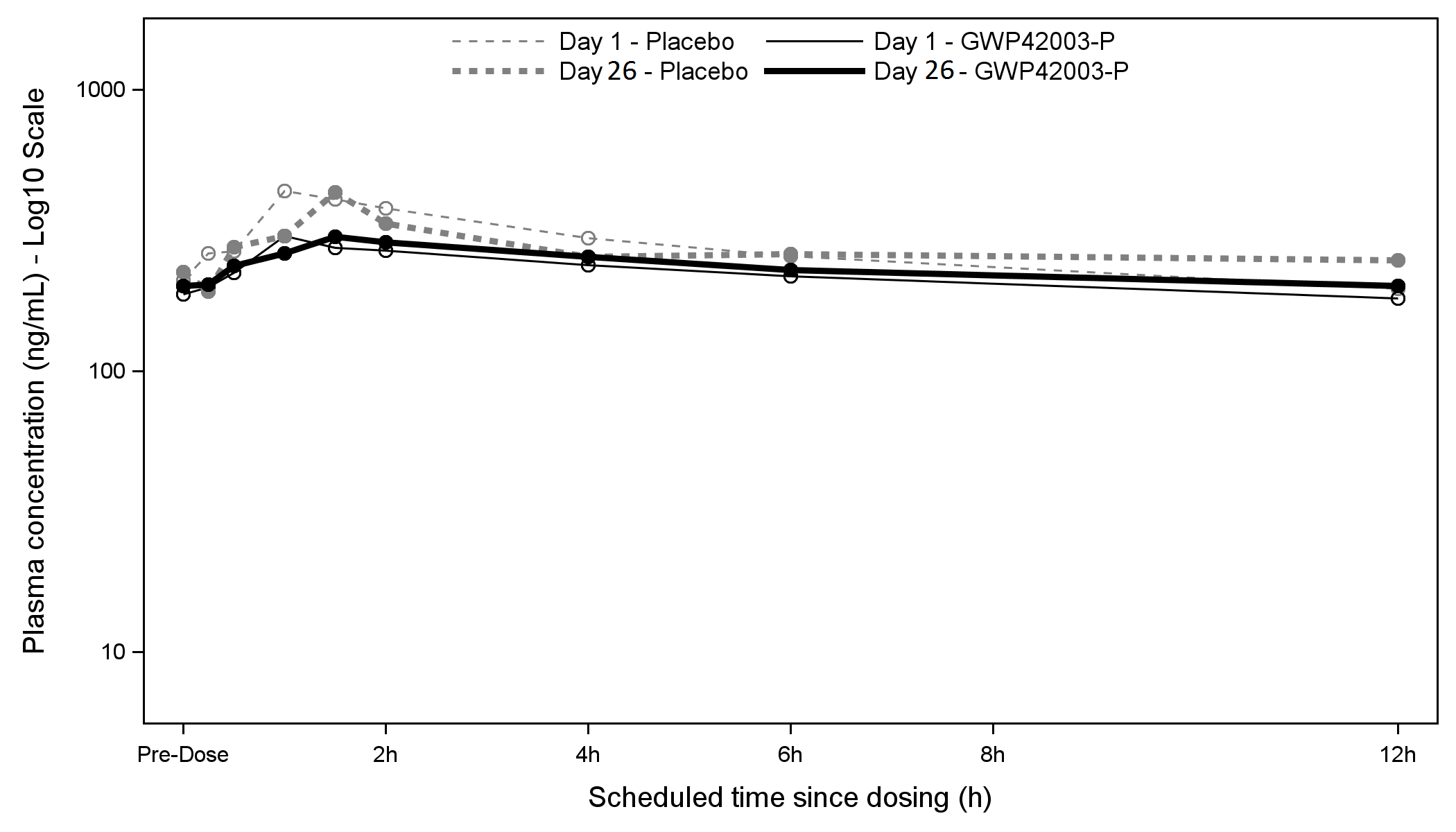
**Programmer’s note:** Only applicable for VPA arm.

8. Pharmacokinetics

8.1. PK Mean Profile

8.1.2b. 4-ene-VPA - Geometric Means - Log10 Scale

PK Population



Source: Table 8.1.5

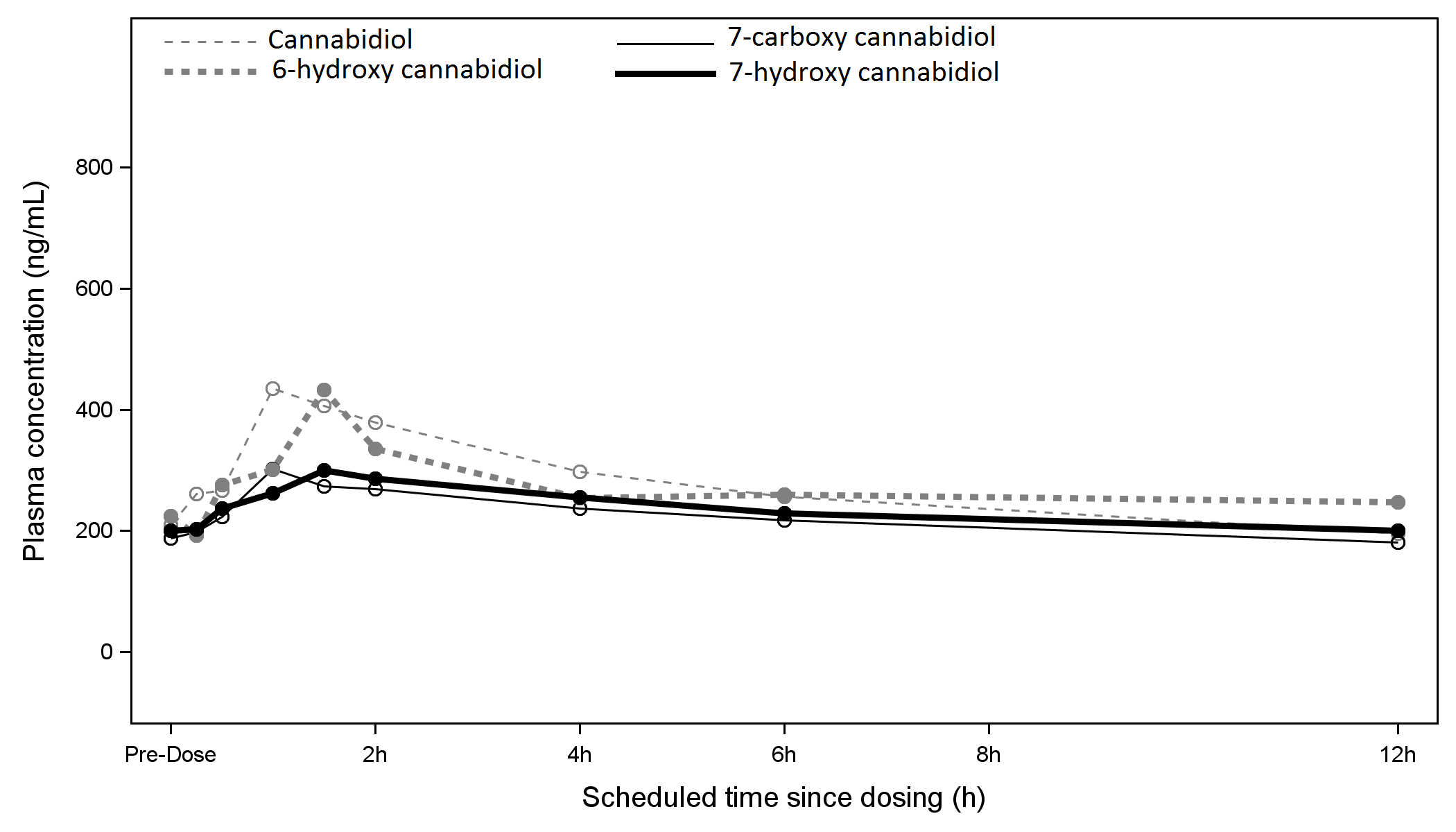
**Programmer’s note:** Only applicable for VPA arm.

8. Pharmacokinetics

8.1. PK Mean Profile

8.1.3a. Cannabidiol and Metabolites - Geometric Means

PK Population



Source: Table 8.1.5

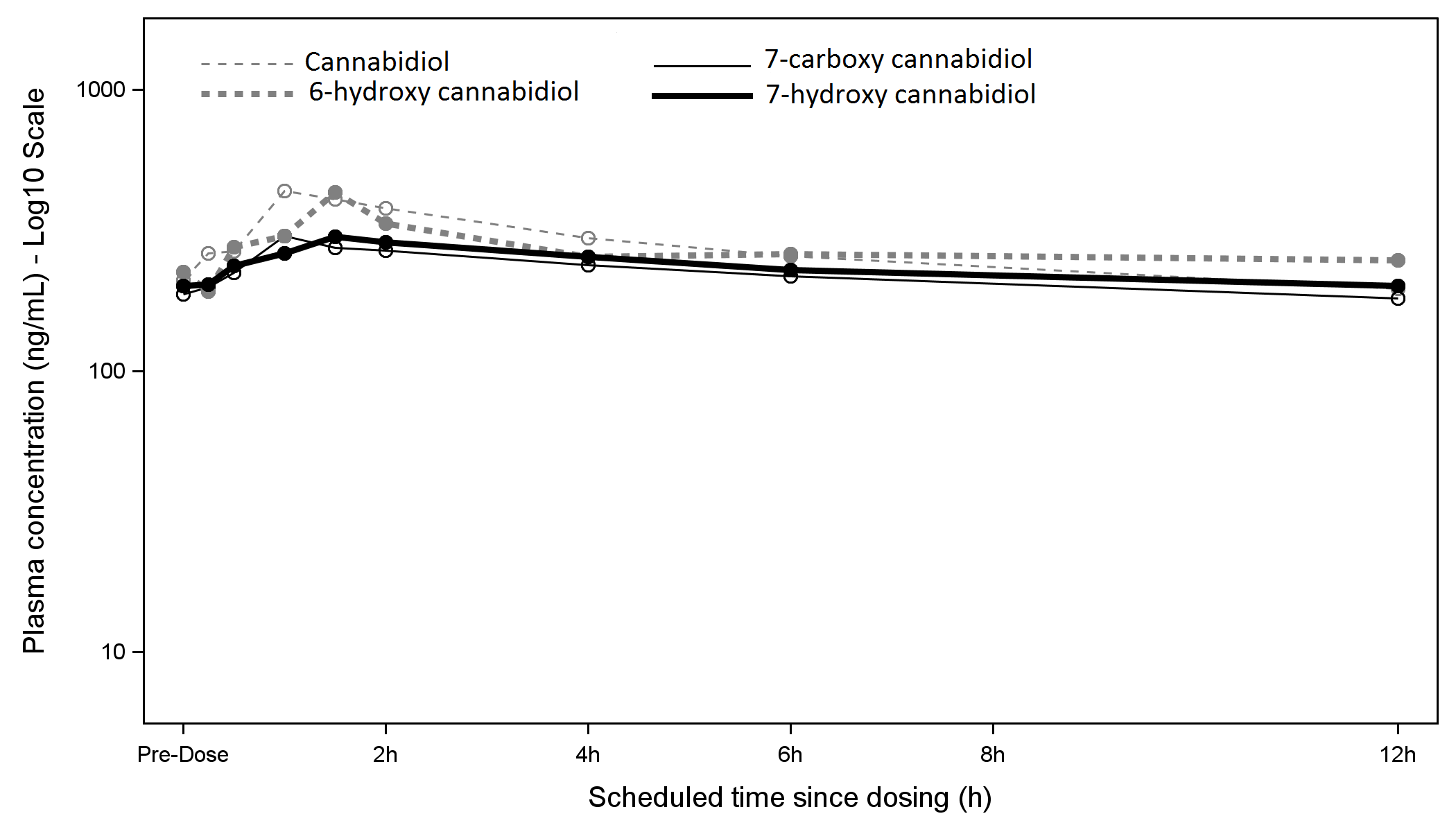
**Programmer’s note:** Only Day 26 for GWP42003-P treatment will be plotted. No line for Placebo will be plotted as all values will be LLOQ. CBD and his three metabolites will be plotted on the same plot.

8. Pharmacokinetics

8.1. PK Mean Profile

8.1.3b. Cannabidiol and Metabolites - Geometric Means - Log10 Scale

PK Population



Source: Table 8.1.5

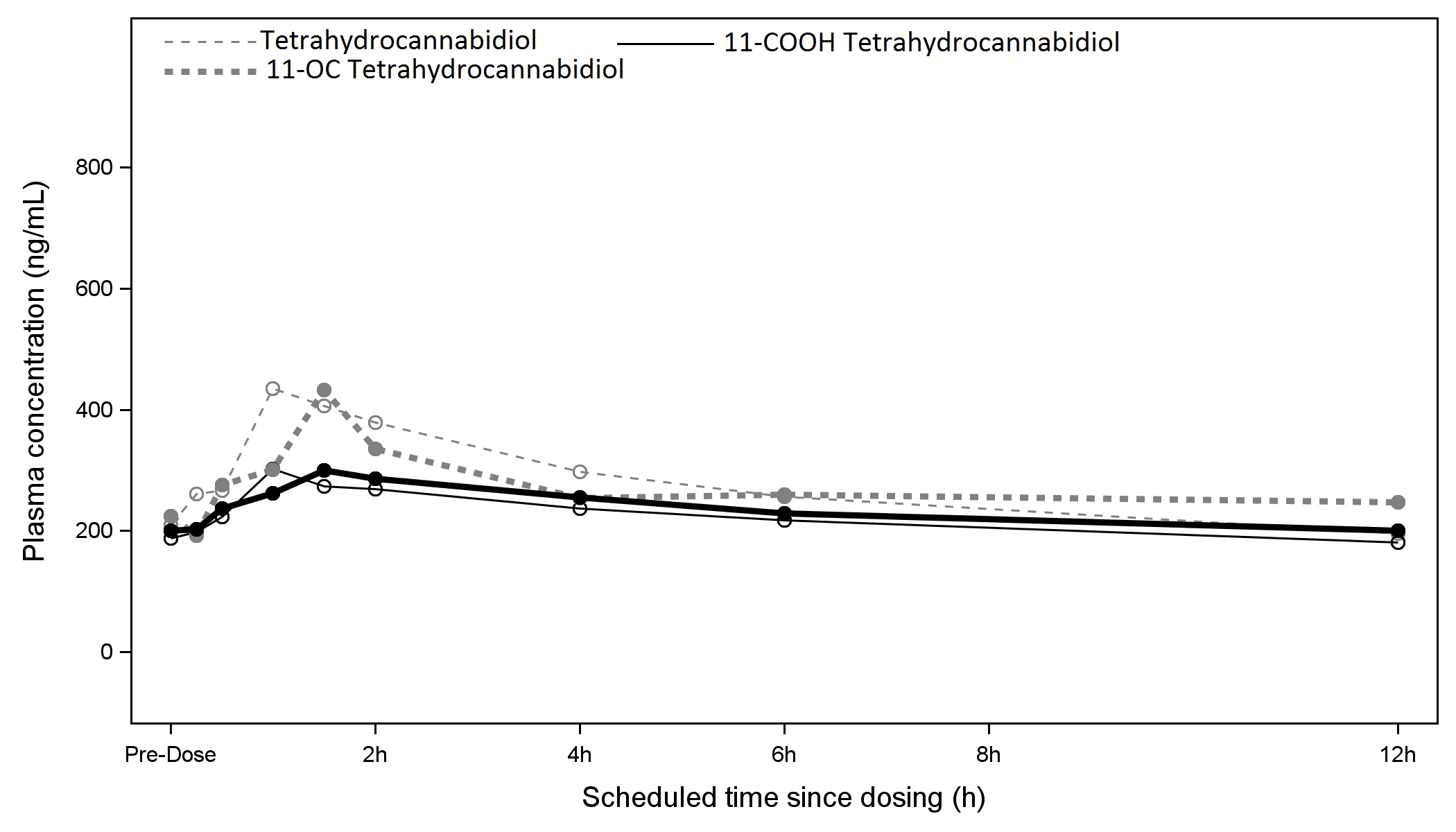
**Programmer’s note:** Only Day 26 for GWP42003-P treatment will be plotted. No line for Placebo will be plotted as all values will be LLOQ. CBD and his three metabolites will be plotted on the same plot.

8. Pharmacokinetics

8.1. PK Mean Profile

8.1.4a. Tetrahydrocannabinol and Metabolites - Geometric Means

PK Population



Source: Table 8.1.5

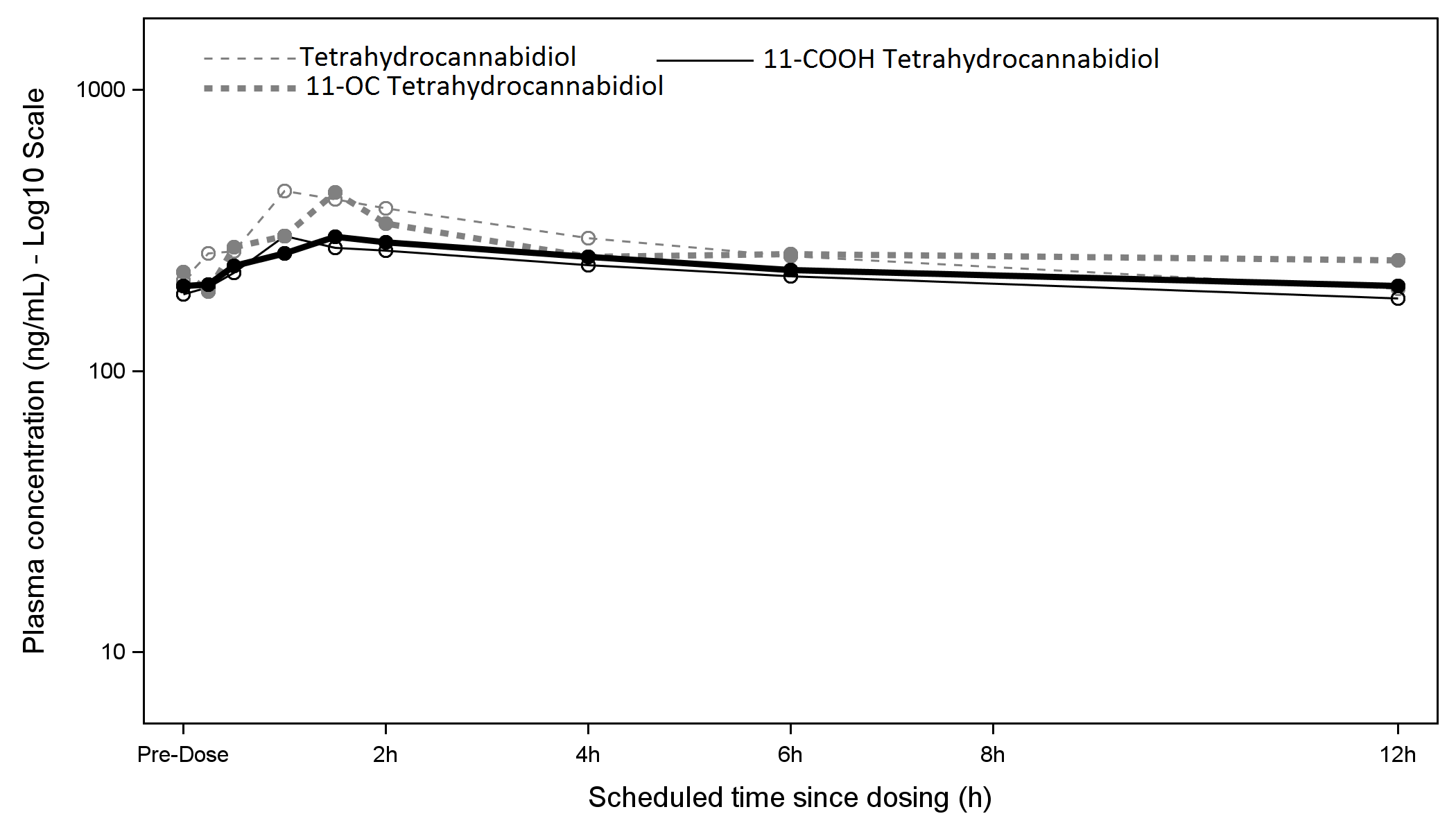
**Programmer’s note:** Only Day 26 for GWP42003-P treatment will be plotted. No line for Placebo will be plotted as all values will be LLOQ. THC and his two metabolites will be plotted on the same plot (so only 3 lines on the plot).

8. Pharmacokinetics

8.1. PK Mean Profile

8.1.4b. Tetrahydrocannabinol and Metabolites - Geometric Means - Log10 Scale

PK Population



Source: Table 8.1.5

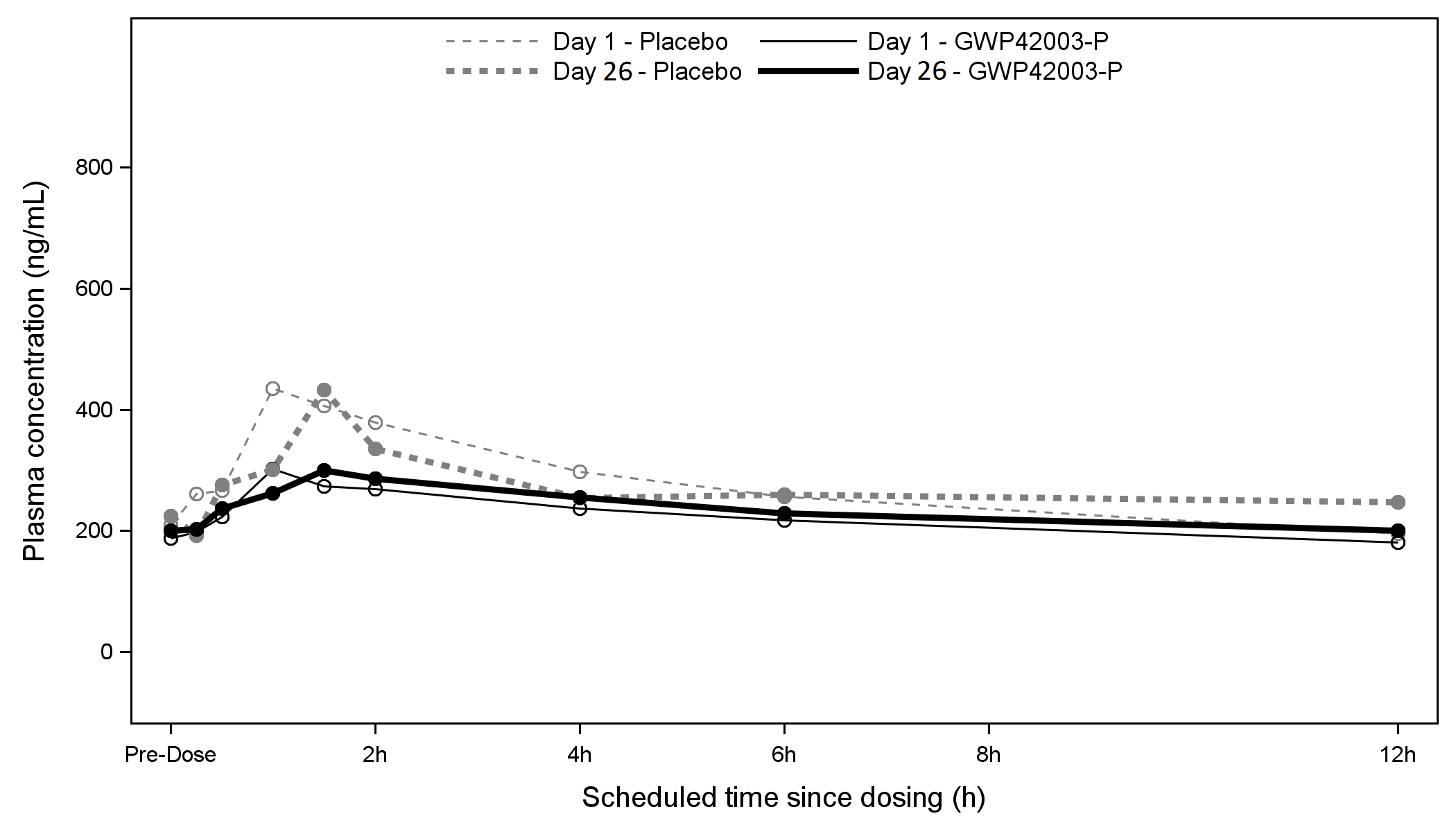
**Programmer’s note:** Only Day 26 for GWP42003-P treatment will be plotted. No line for Placebo will be plotted as all values will be LLOQ. THC and his two metabolites will be plotted on the same plot (so only 3 lines on the plot).

8. Pharmacokinetics

8.1. PK Mean Profile

8.1.5a. Clobazam - Geometric Means

PK Population



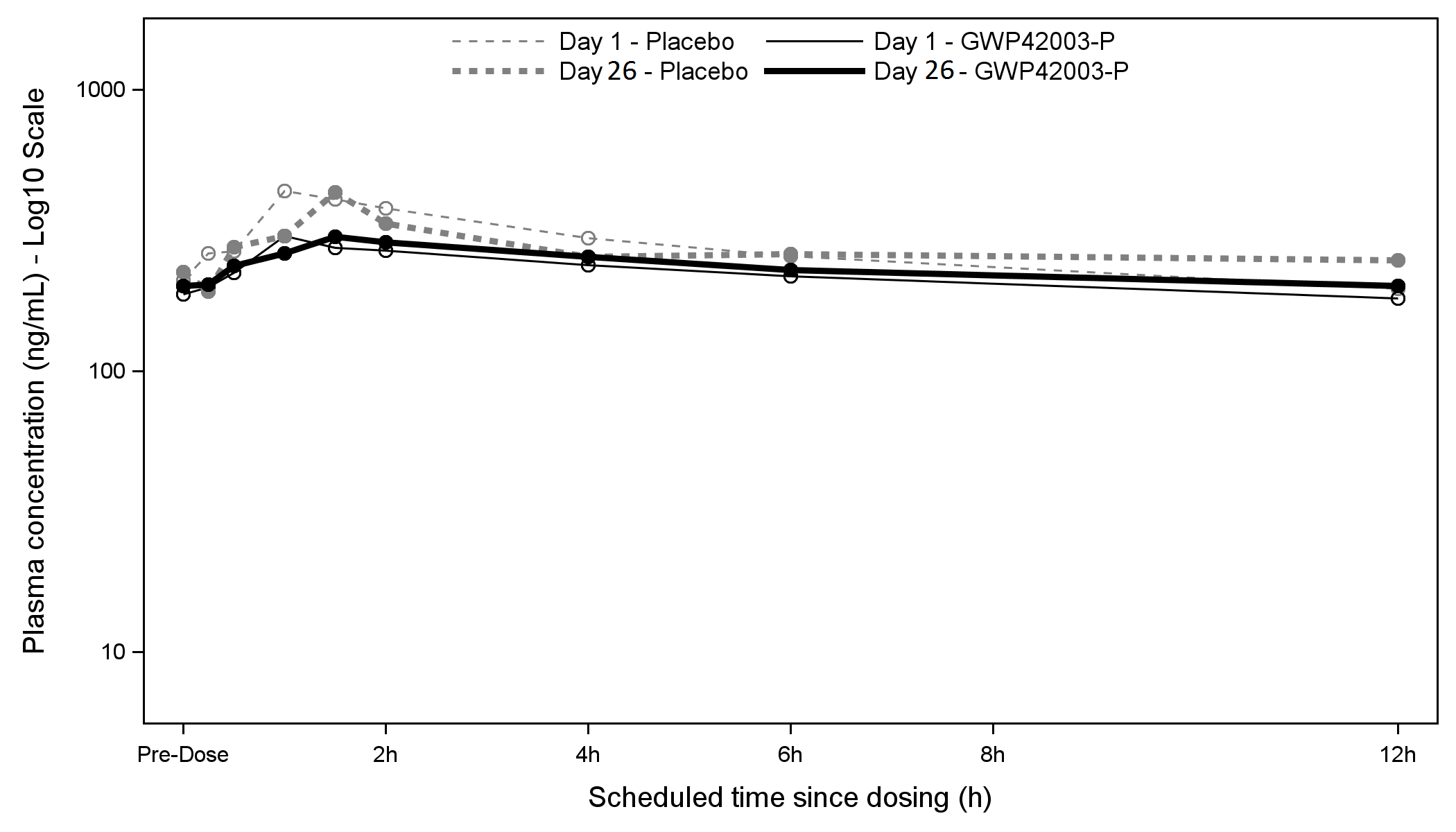
Source: Table 8.1.5

8. Pharmacokinetics

8.1. PK Mean Profile

8.1.5b. Clobazam - Geometric Means - Log10 Scale

PK Population



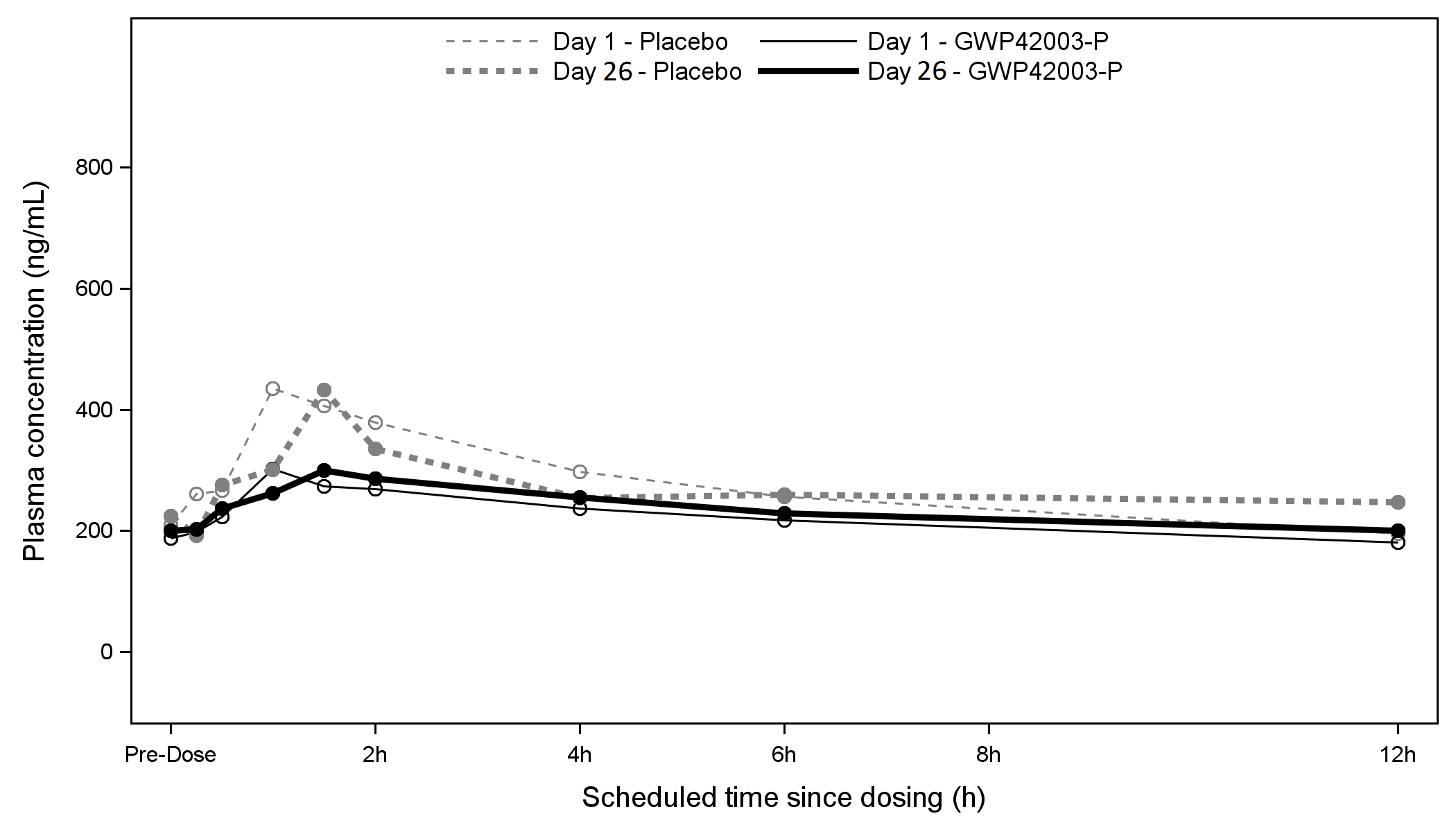
Source: Table 8.1.5

8. Pharmacokinetics

8.1. PK Mean Profile

8.1.6a. N-Desmethylclobazam - Geometric Means

PK Population



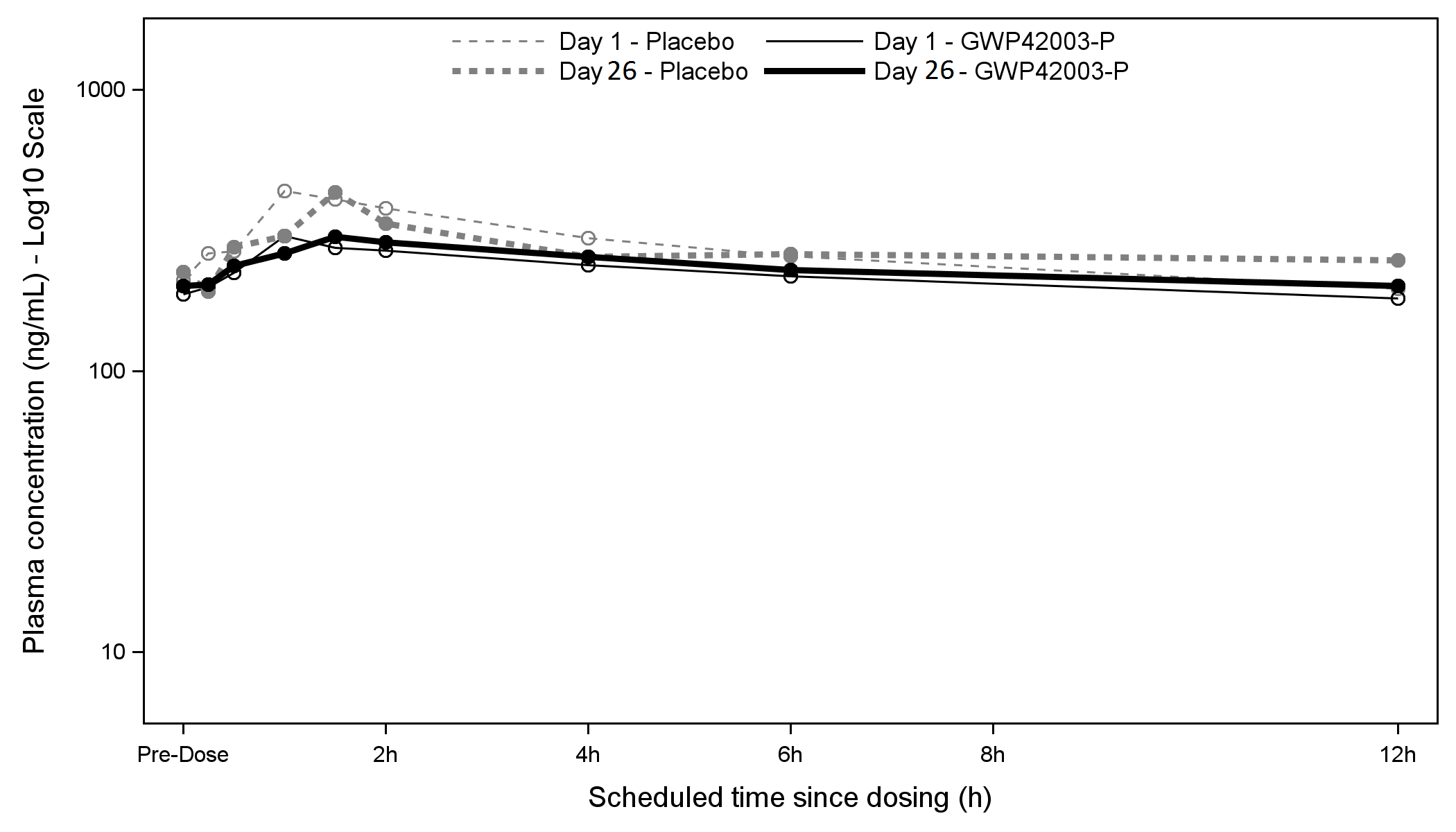
Source: Table 8.1.5

8. Pharmacokinetics

8.1. PK Mean Profile

8.1.6b. N-Desmethylclobazam - Geometric Means - Log10 Scale

PK Population



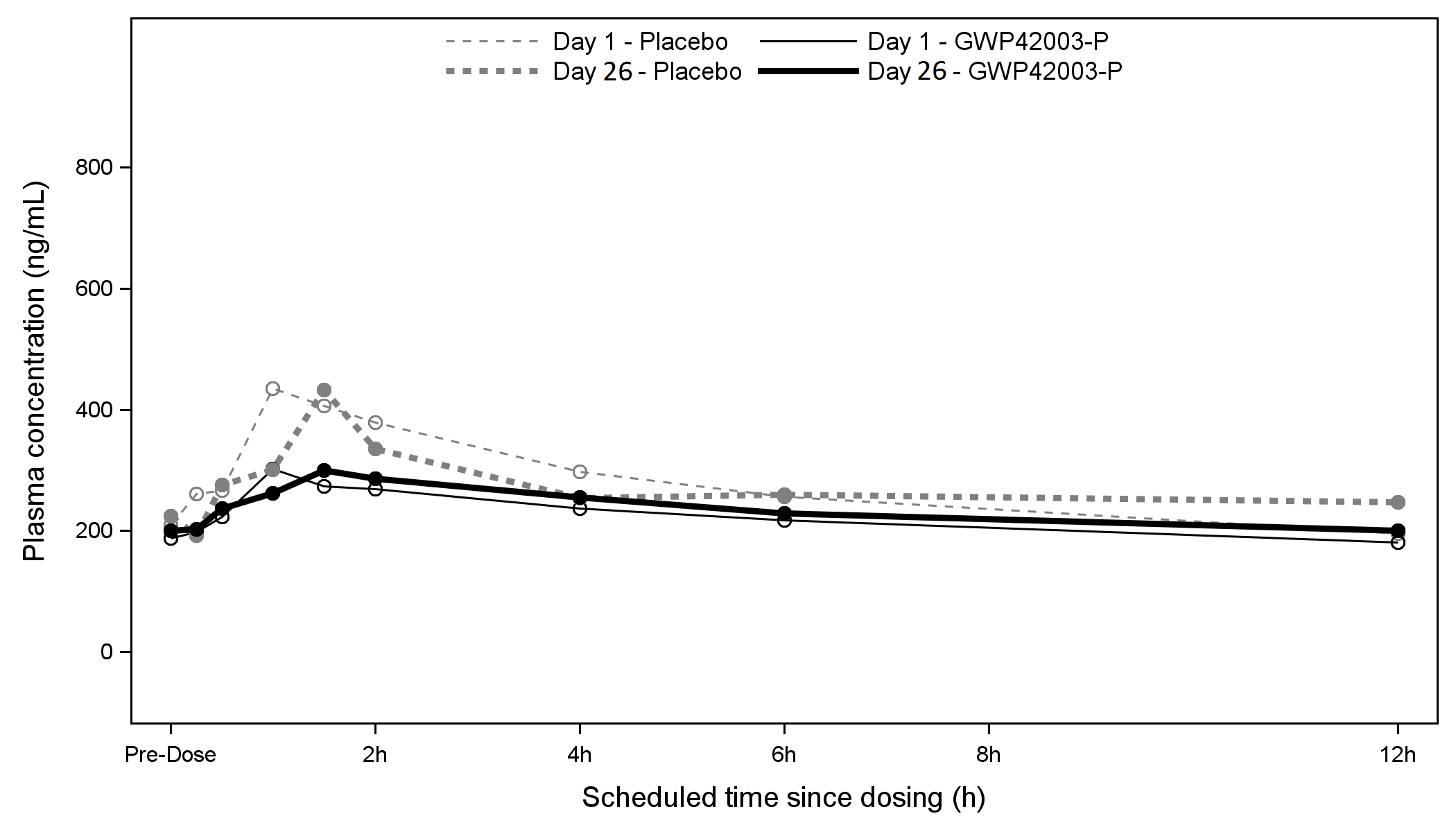
Source: Table 8.1.5

8. Pharmacokinetics

8.1. PK Mean Profile

8.1.7a. Levetiracetam - Geometric Means

PK Population



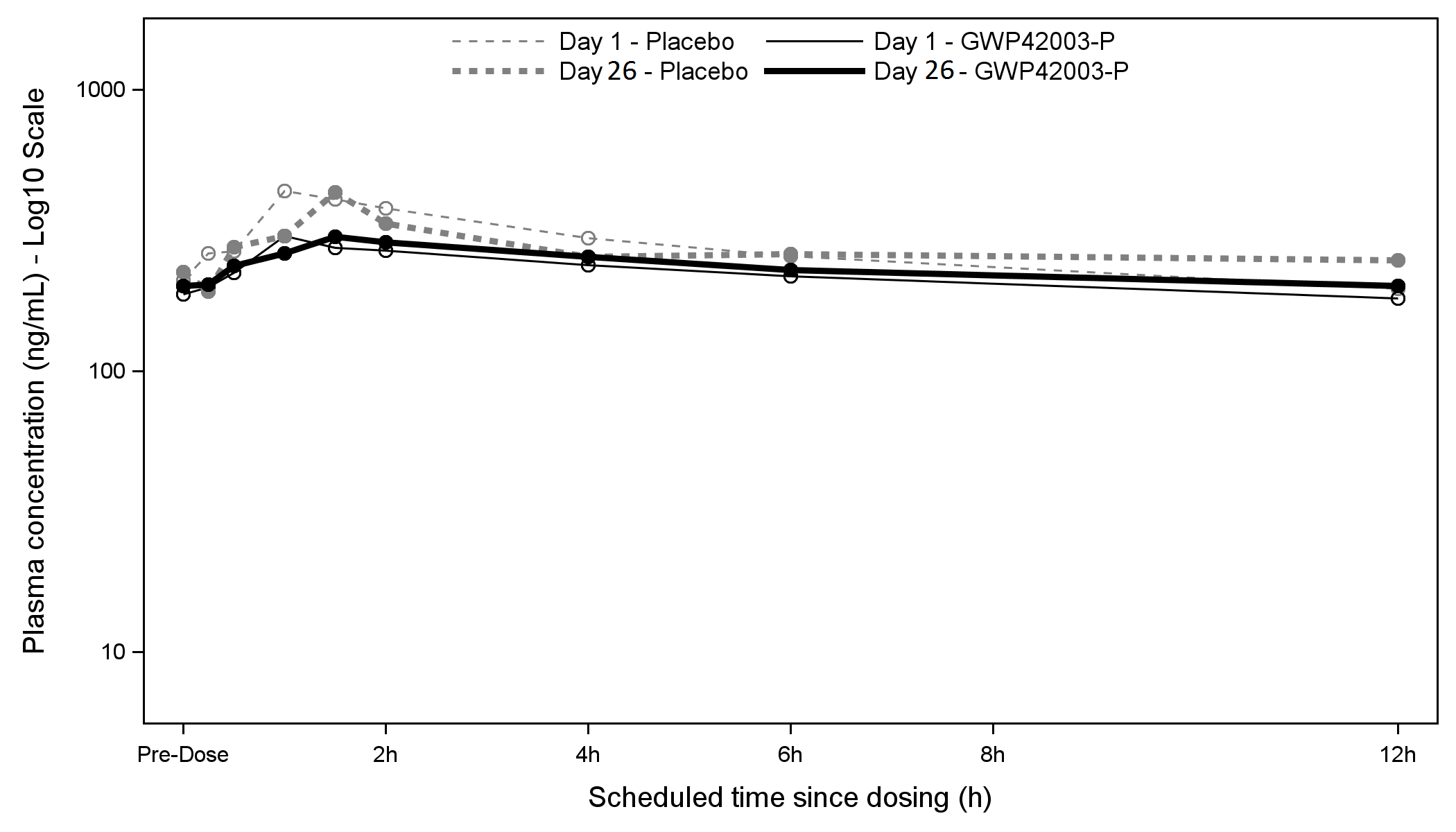
Source: Table 8.1.5

8. Pharmacokinetics

14-1. PK Mean Profile

8.1.7b. Levetiracetam - Geometric Means - Log10 Scale

PK Population



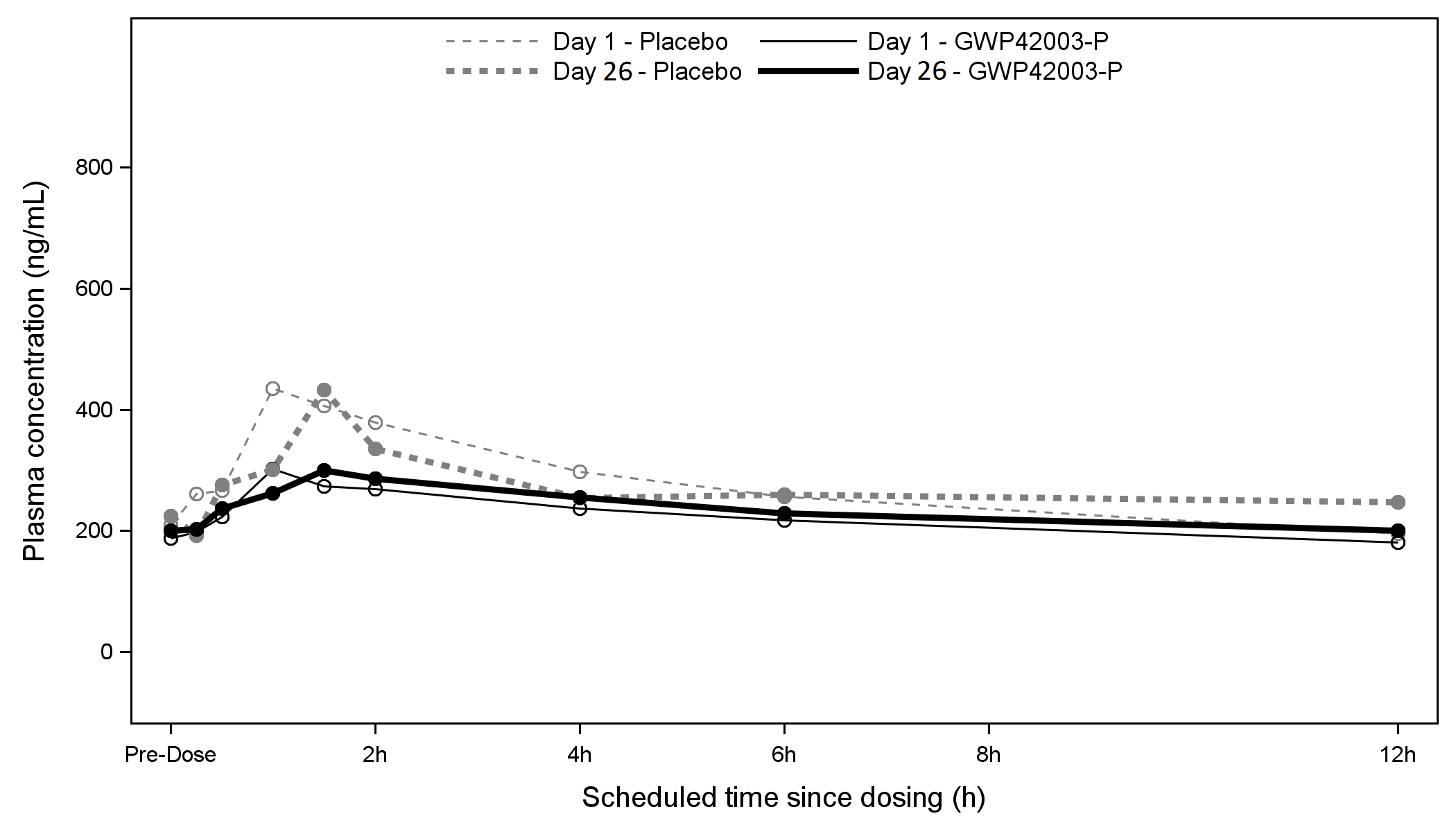
Source: Table 8.1.5

8. Pharmacokinetics

14-2. PK Mean Profile

8.1.8a. Topiramate - Geometric Means

PK Population



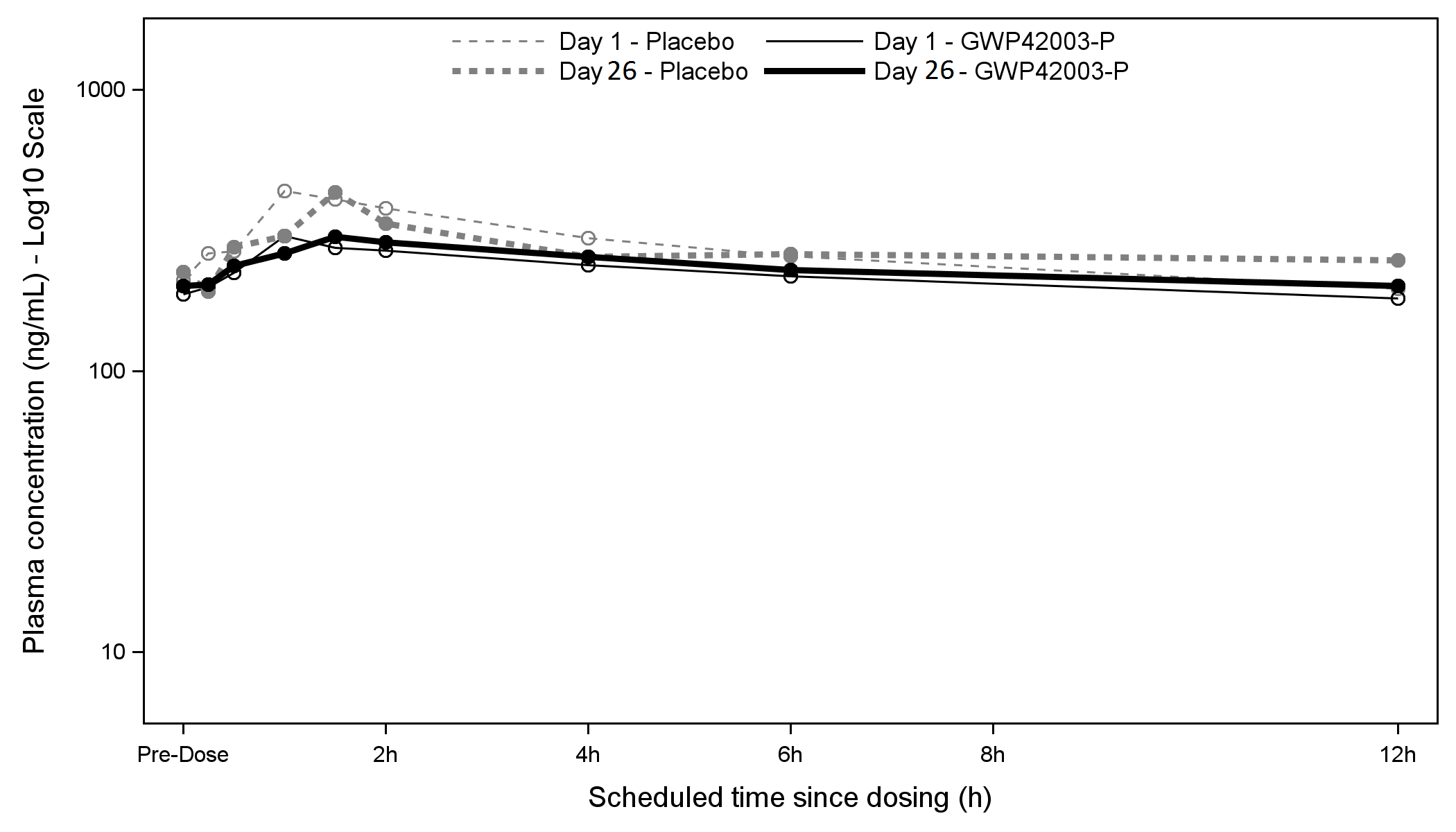
Source: Table 8.1.5

8. Pharmacokinetics

8.1. PK Mean Profile

8.1.8b. Topiramate - Geometric Means - Log10 Scale

PK Population



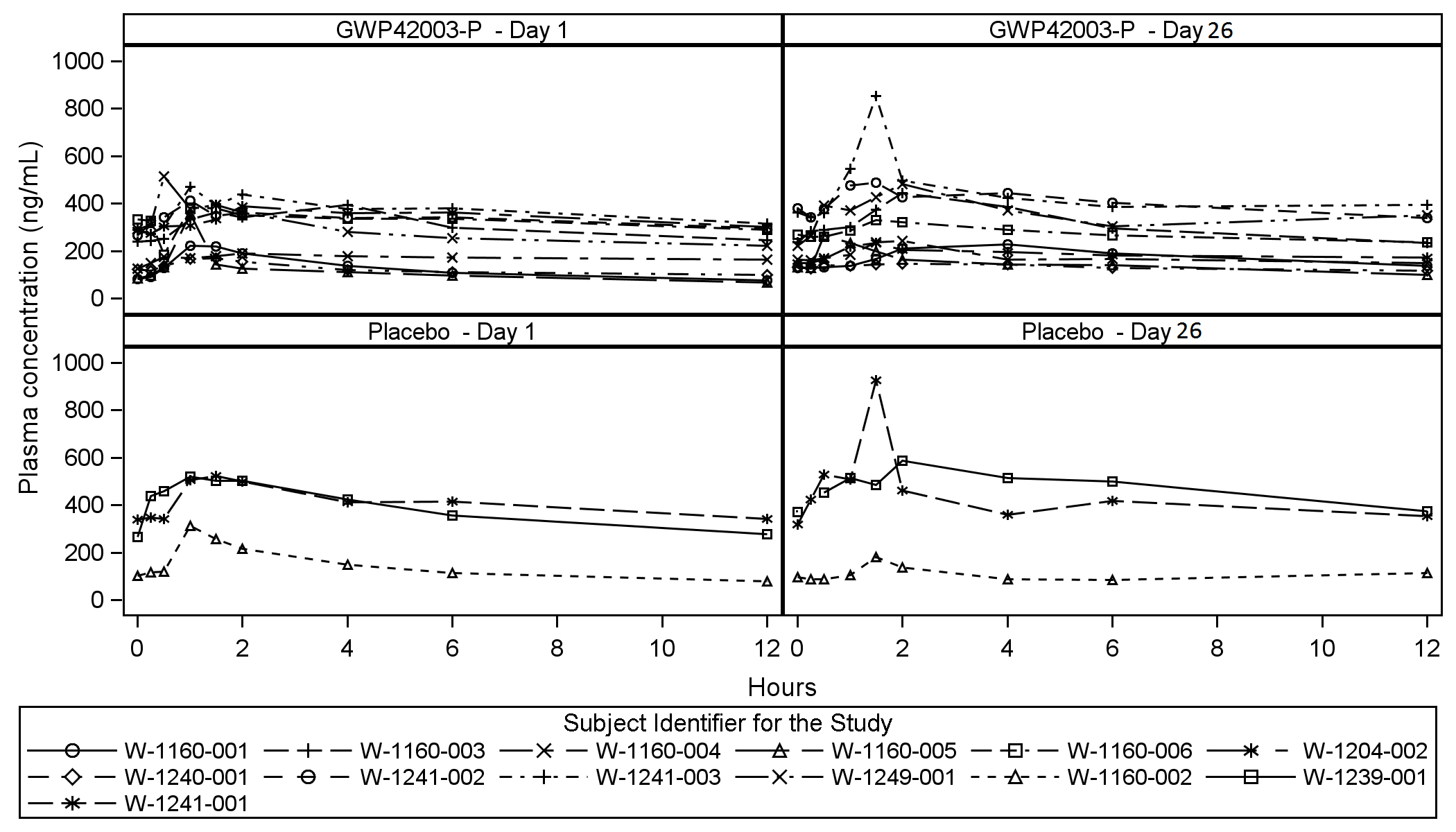
Source: Table 8.1.5

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.1a. Stiripentol

PK Population



Source: Listing 8.1

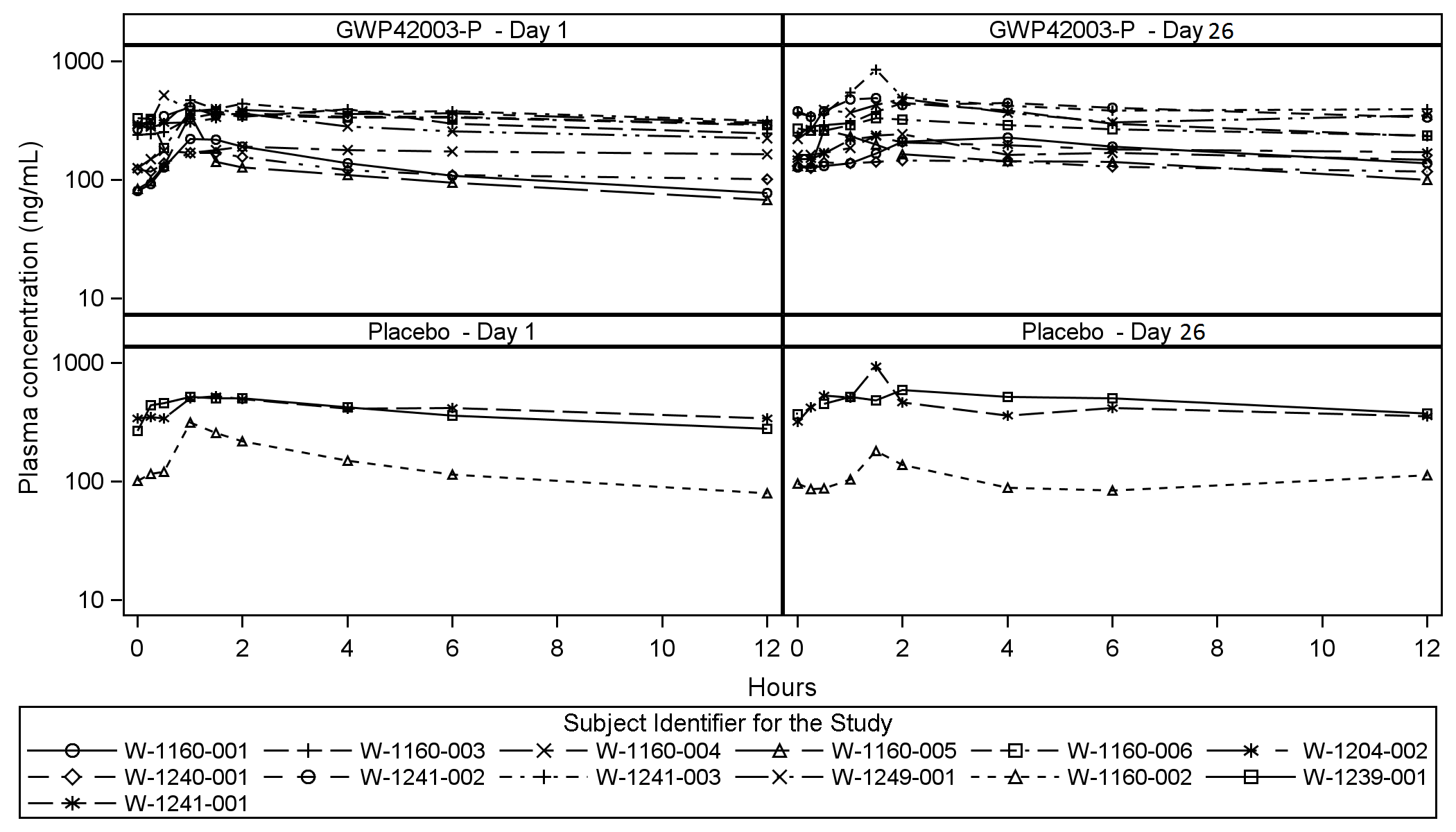
**Programmer’s note:** This title is applicable for STP arm. For VPA arm that will be “8.2.1a. Valproic Acid”.

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.1b. Stiripentol - Log10 Scale

PK Population



Source: Listing 8.1

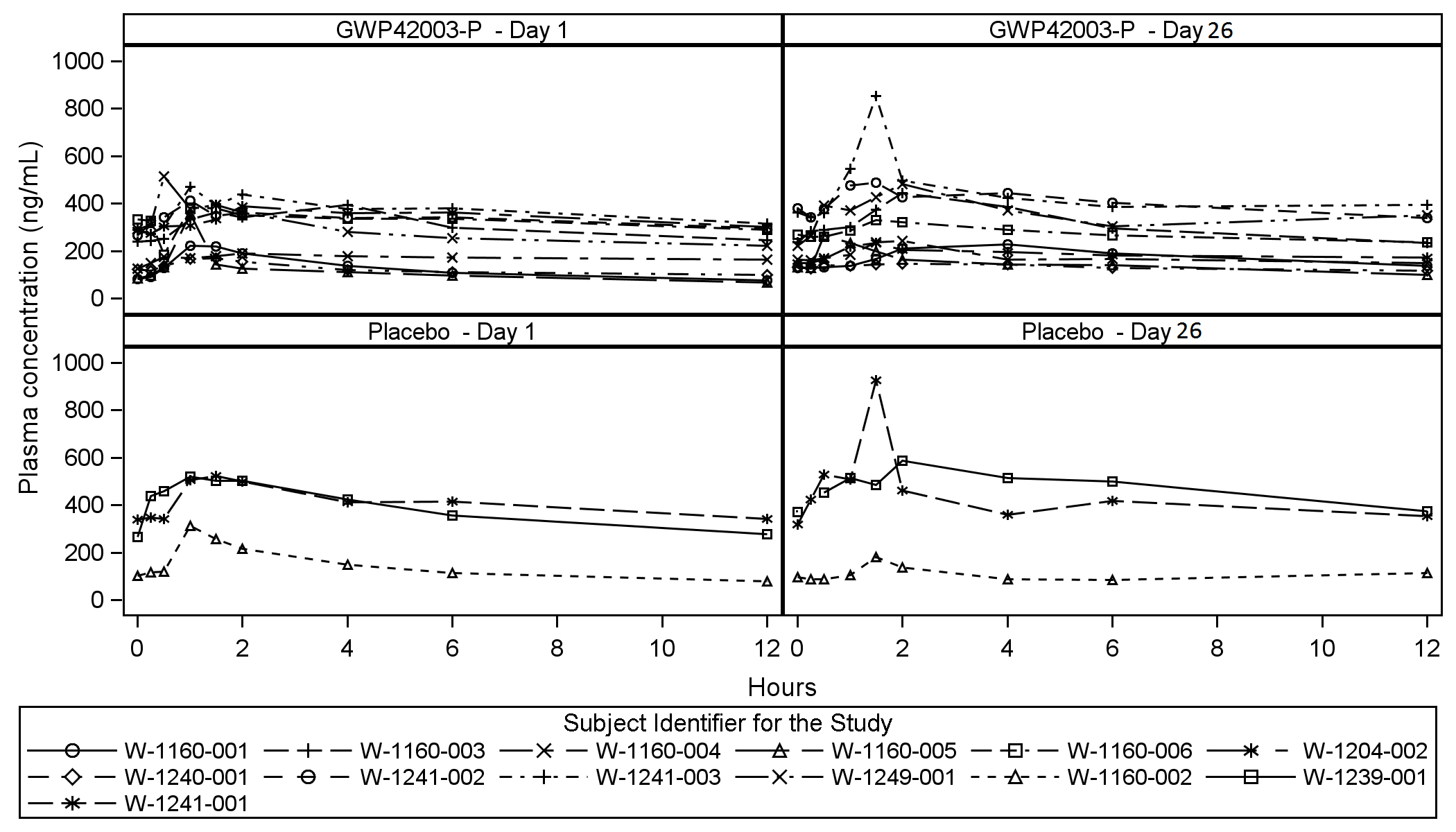
**Programmer’s note:** This title is applicable for STP arm. For VPA arm that will be “8.2.1b. Valproic Acid - Log10 Scale”.

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.2a. 4-ene-VPA

PK Population



Source: Listing 8.1

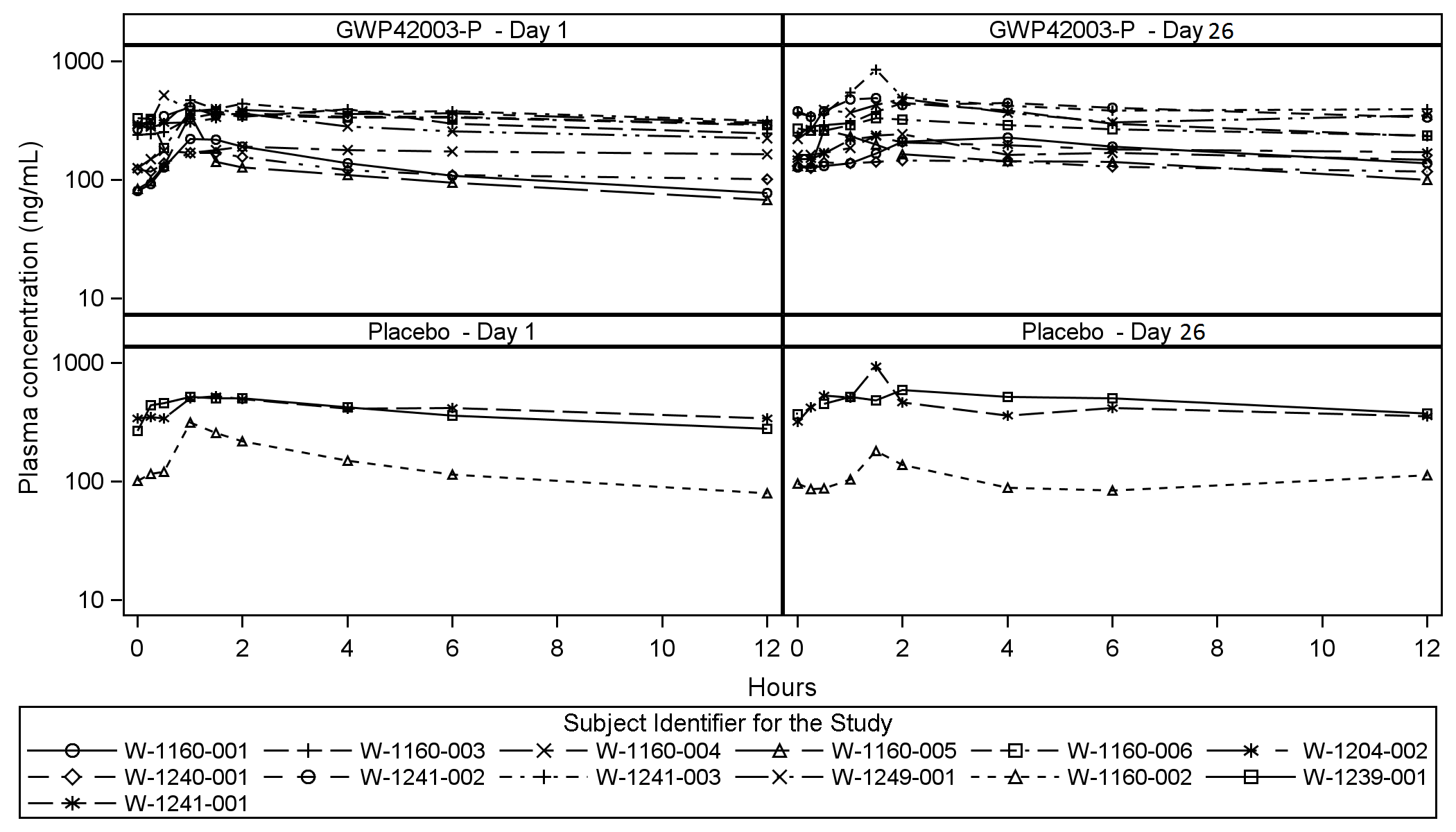
**Programmer’s note:** Only applicable for VPA arm.

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.2b. 4-ene-VPA - Log10 Scale

PK Population



Source: Listing 8.1

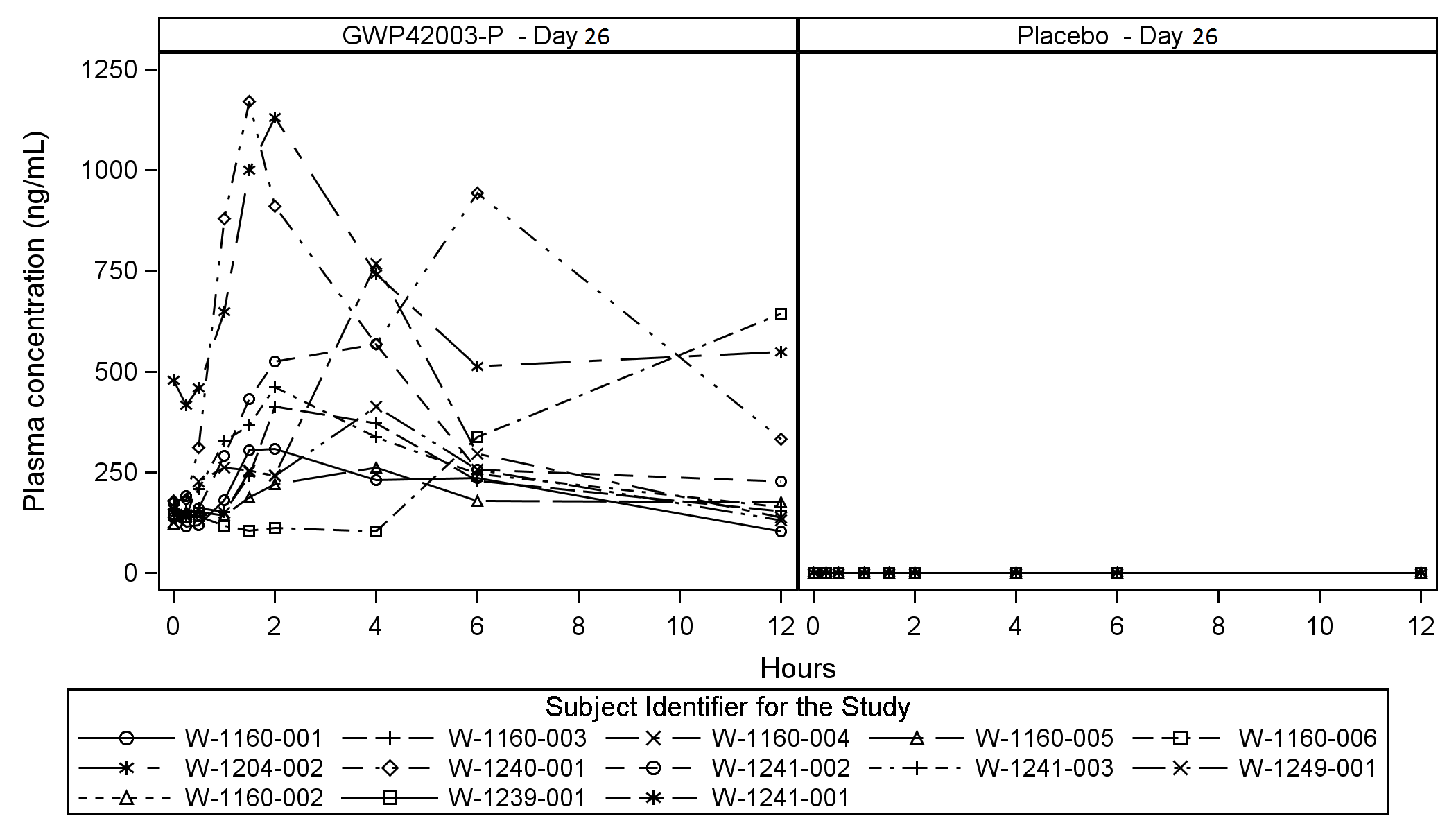
**Programmer’s note:** Only applicable for VPA arm.

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.3a. Cannabidiol

PK Population



Source: Listing 8.1

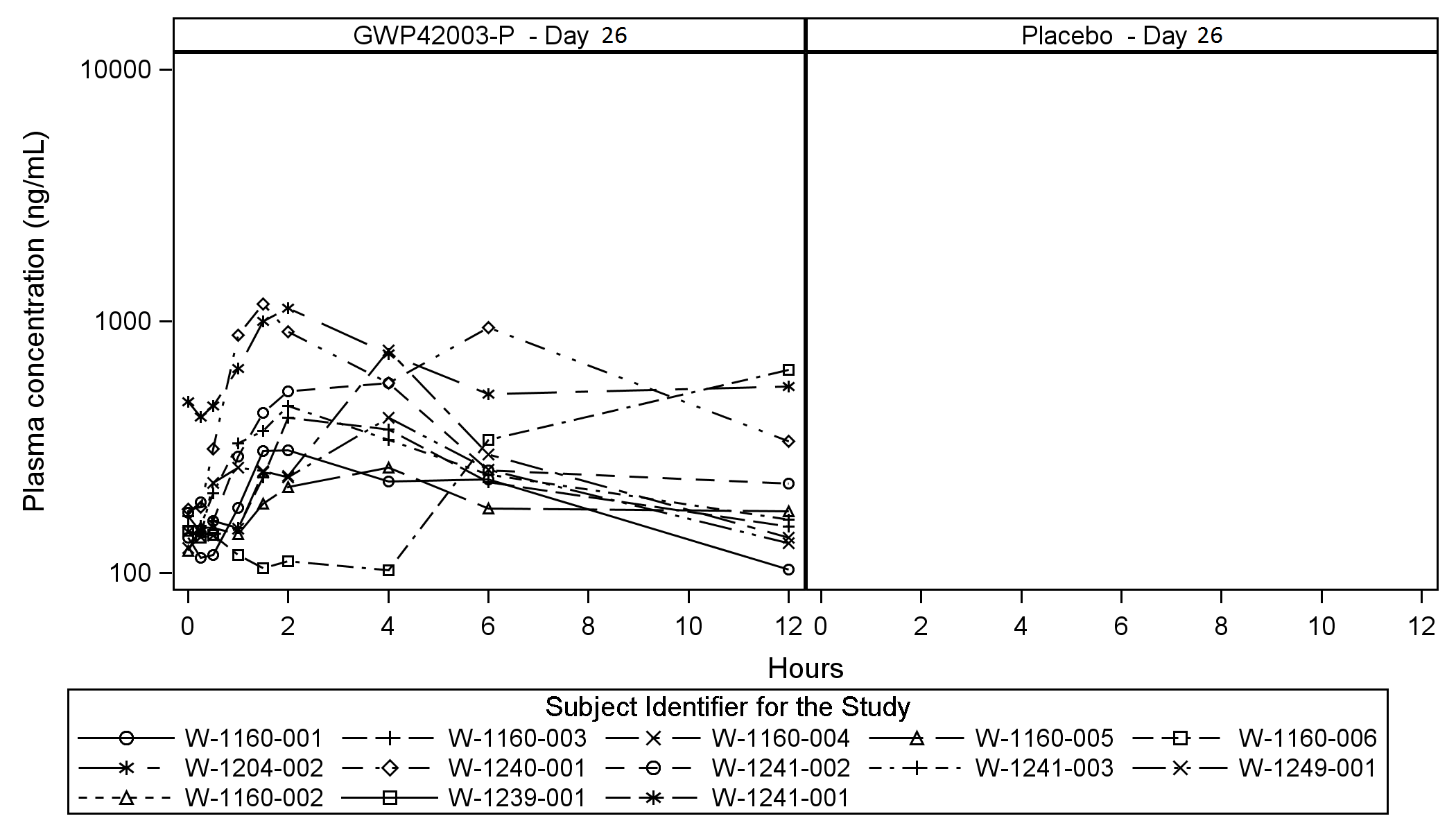
**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.3b. Cannabidiol - Log10 Scale

PK Population



Source: Listing 8.1

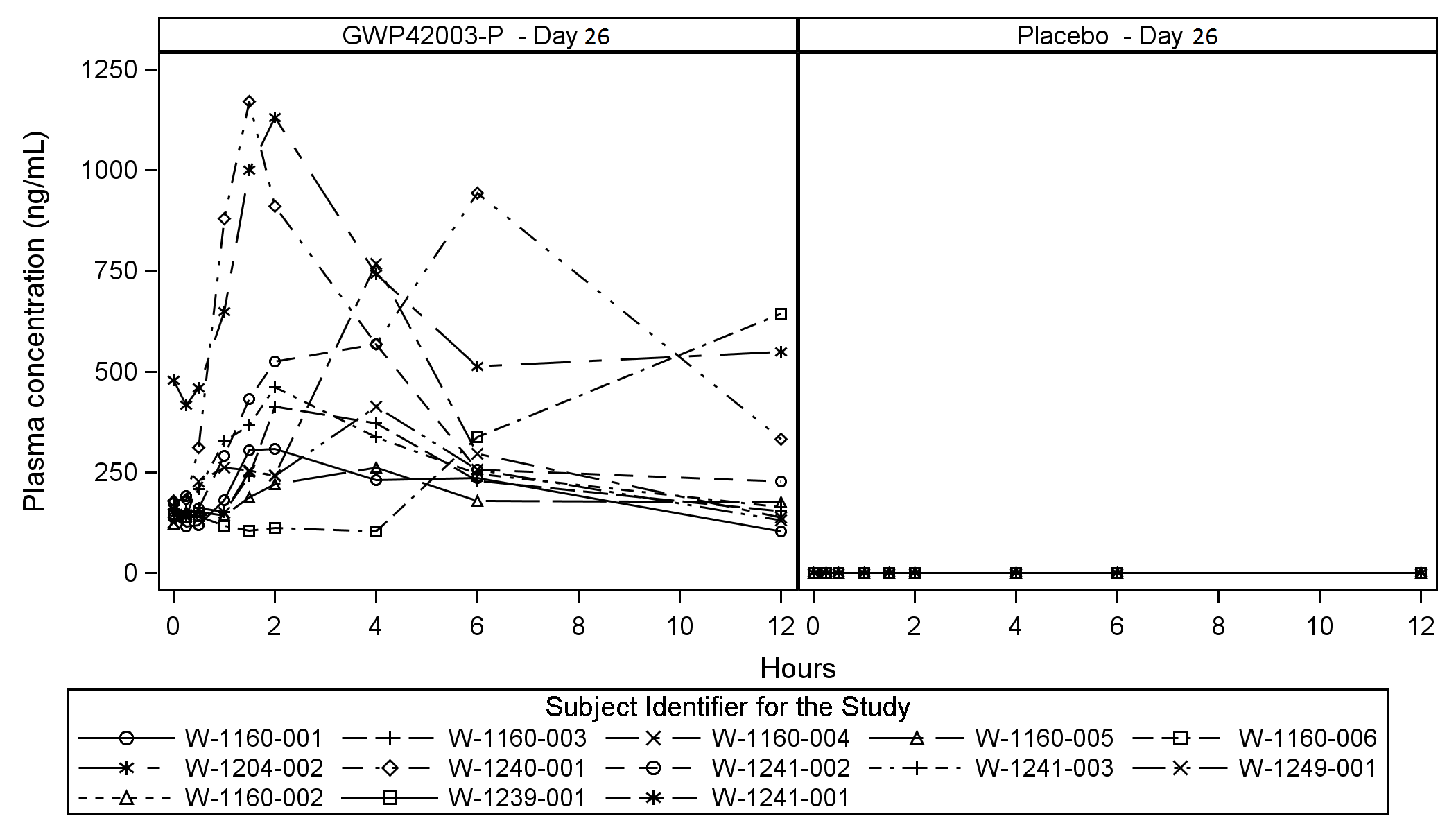
**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.4a. 6-hydroxy cannabidiol

PK Population



Source: Listing 8.1

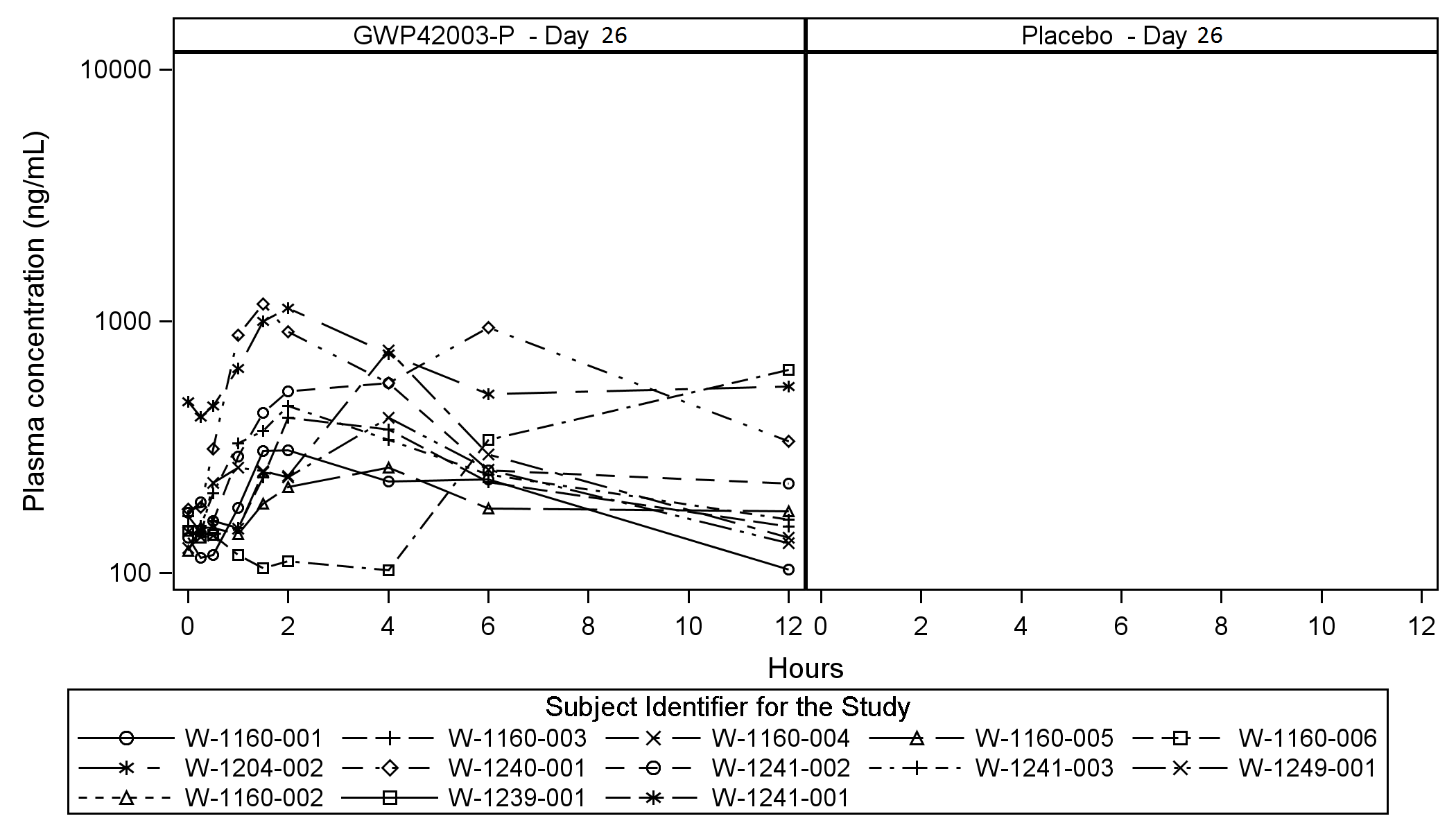
**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.4b. 6-hydroxy cannabidiol - Log10 Scale

PK Population



Source: Listing 8.1

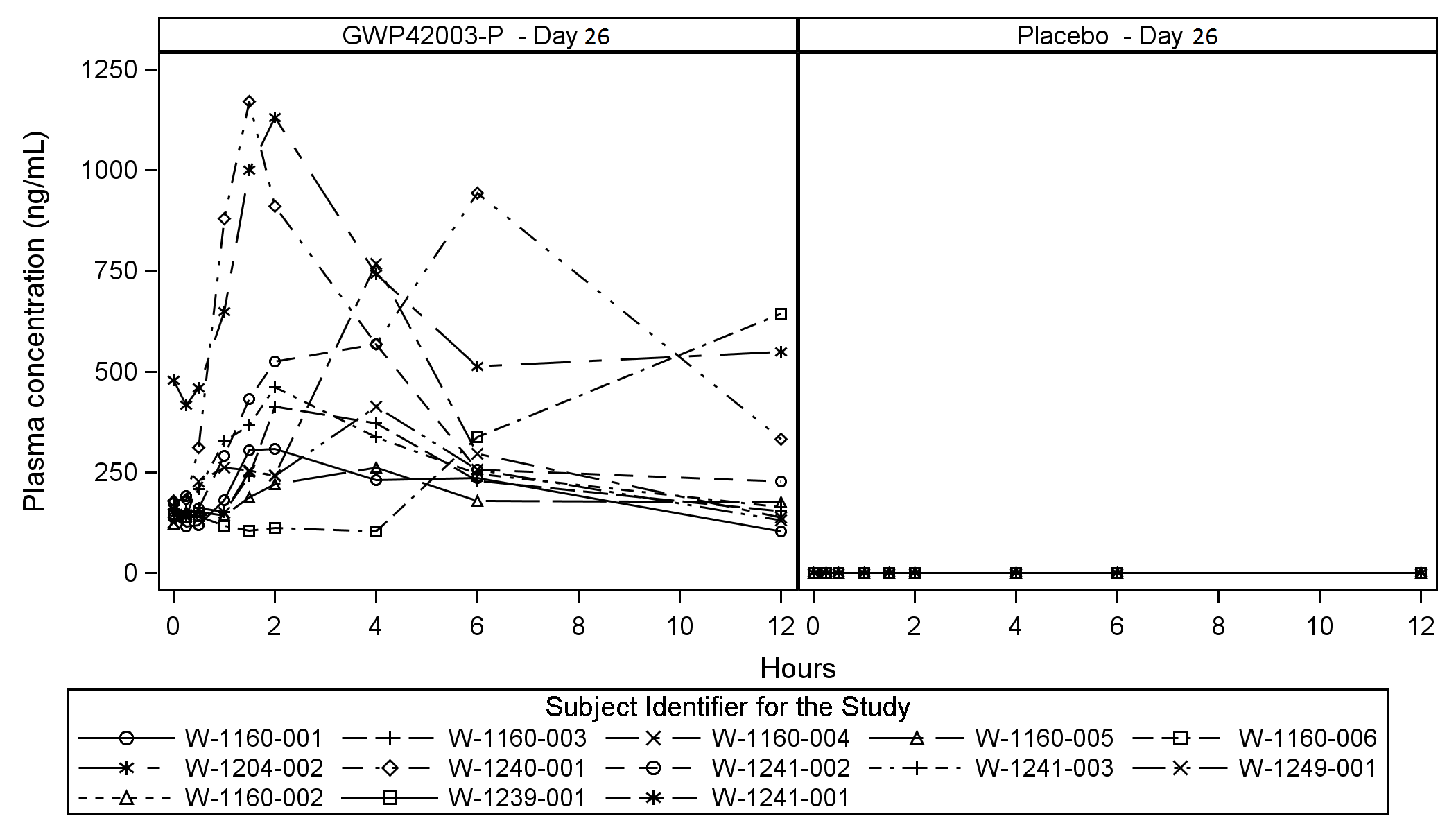
**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.5a. 7-carboxy cannabidiol

PK Population



Source: Listing 8.1

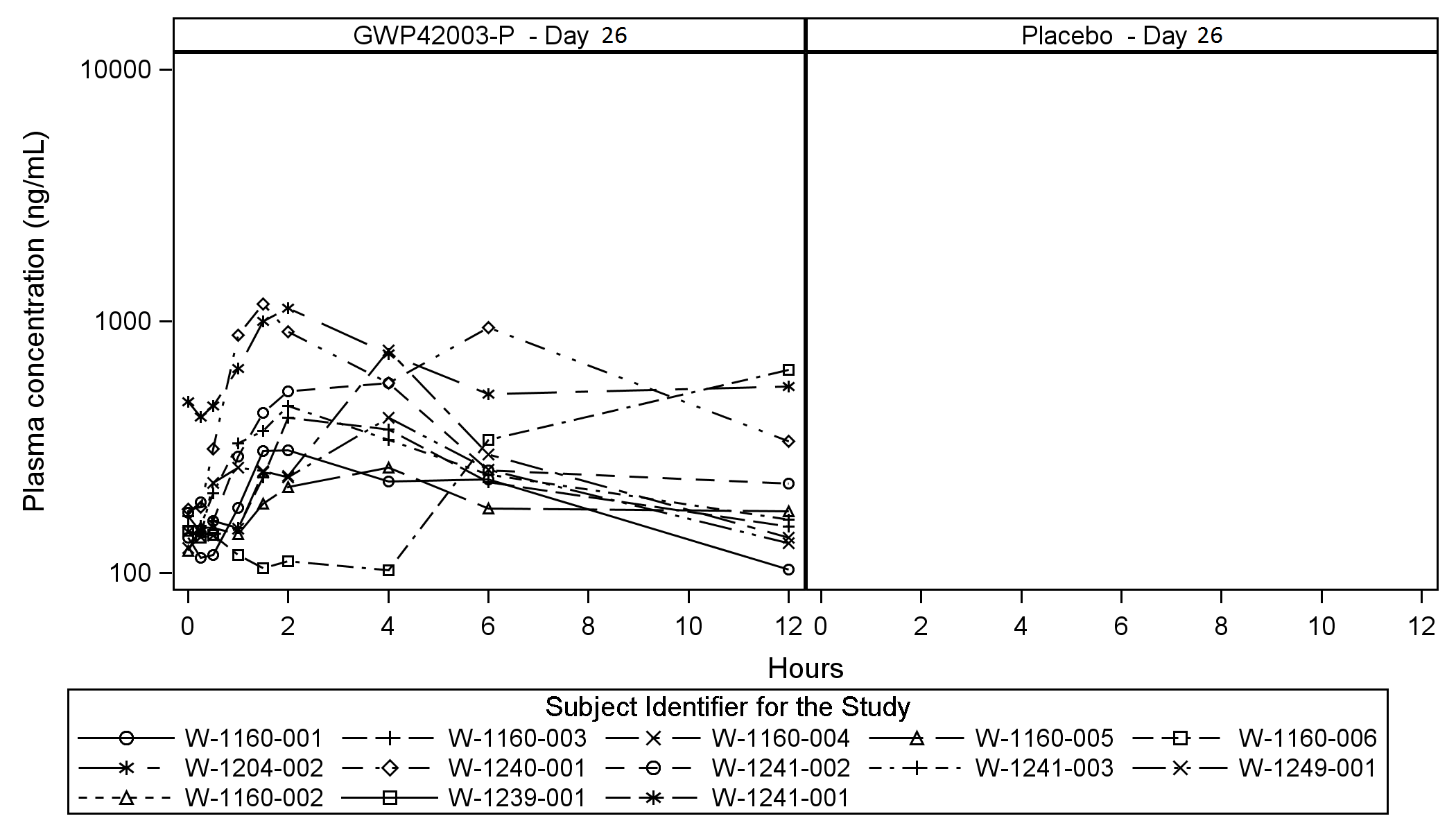
**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.5b. 7-carboxy cannabidiol - Log10 Scale

PK Population



Source: Listing 8.1

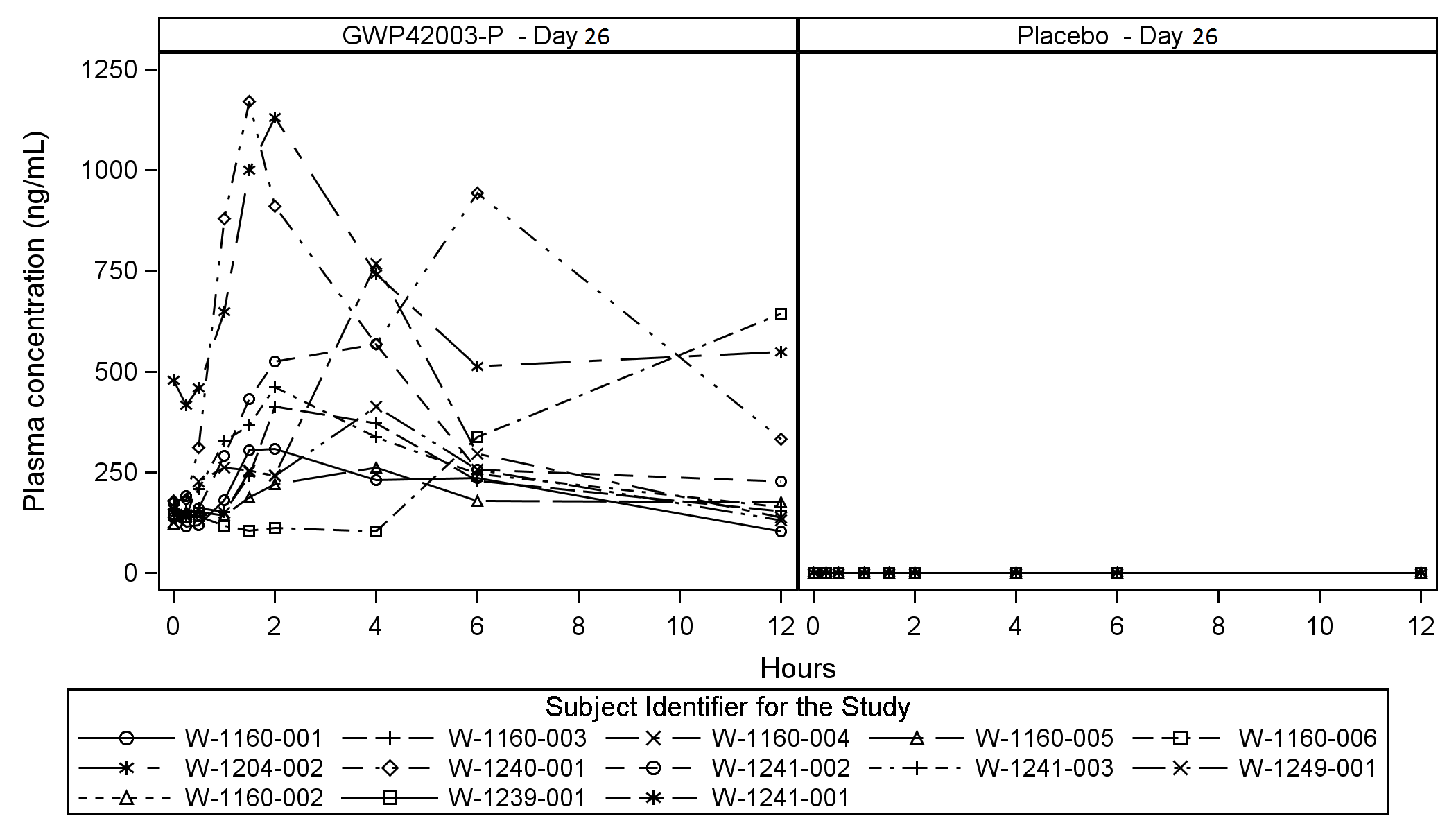
**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.6a. 7-hydroxy cannabidiol

PK Population



Source: Listing 8.1

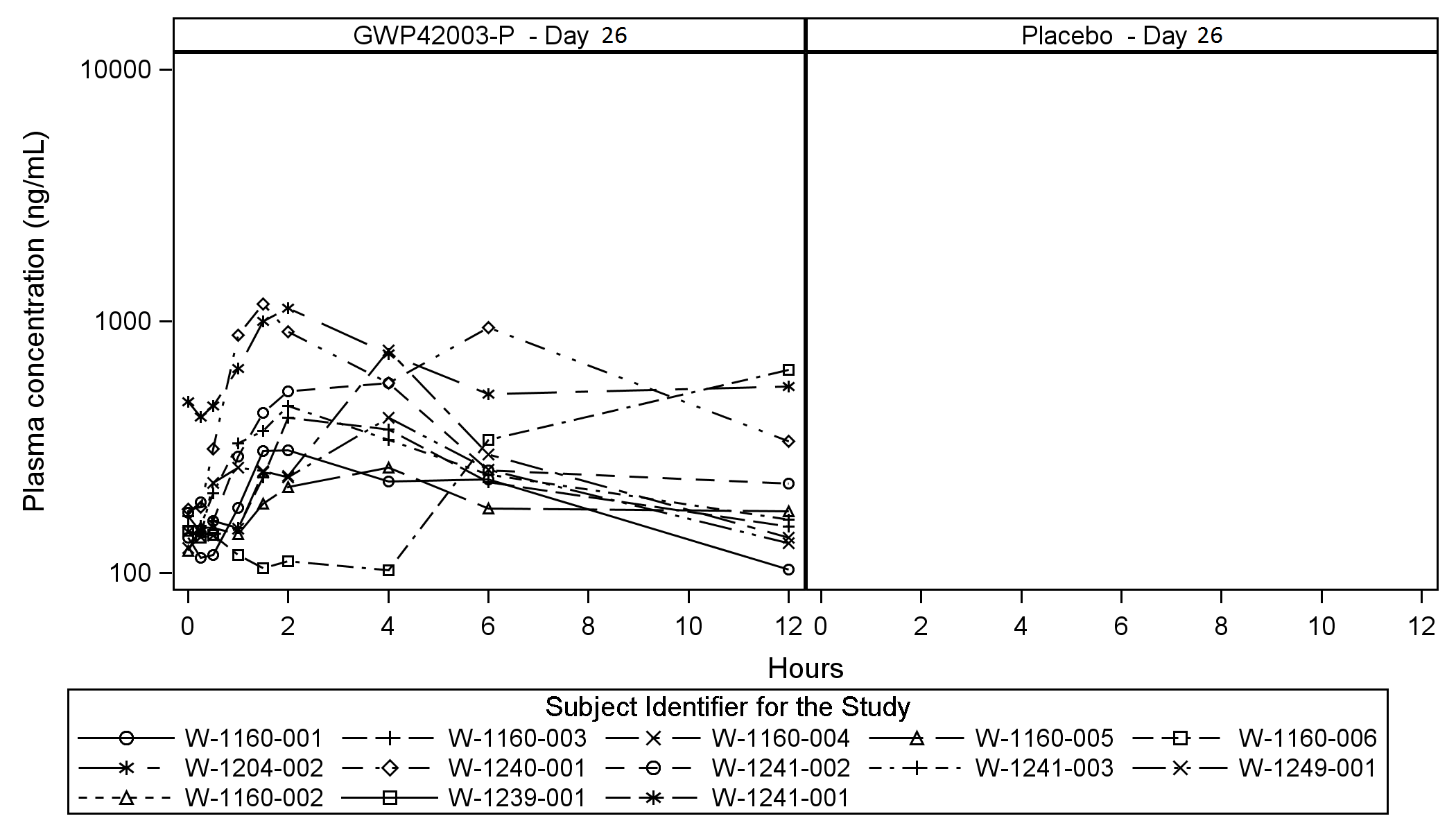
**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.6b. 7-hydroxy cannabidiol - Log10 Scale

PK Population



Source: Listing 8.1

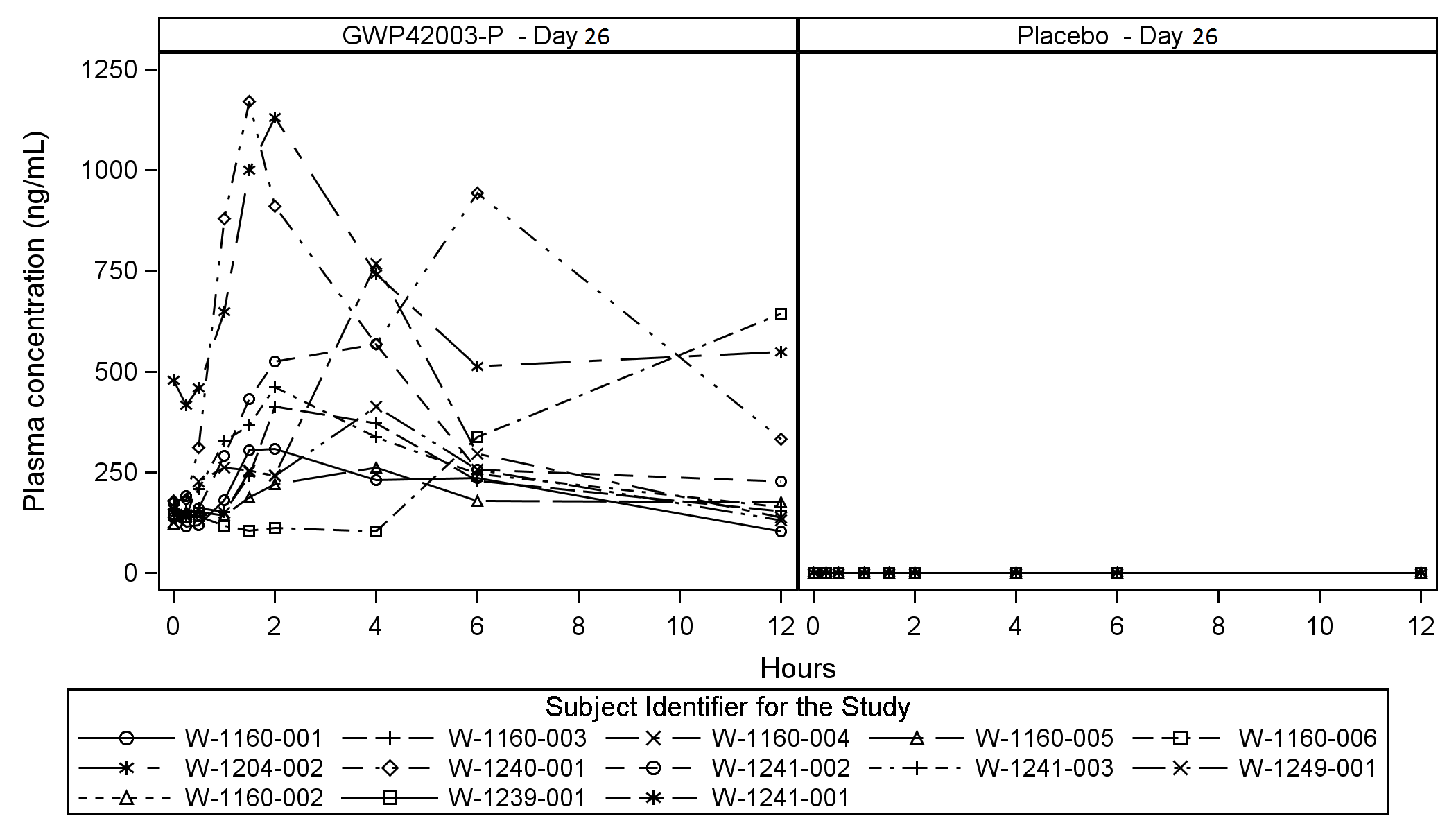
**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.7a. Tetrahydrocannabinol

PK Population



Source: Listing 8.1

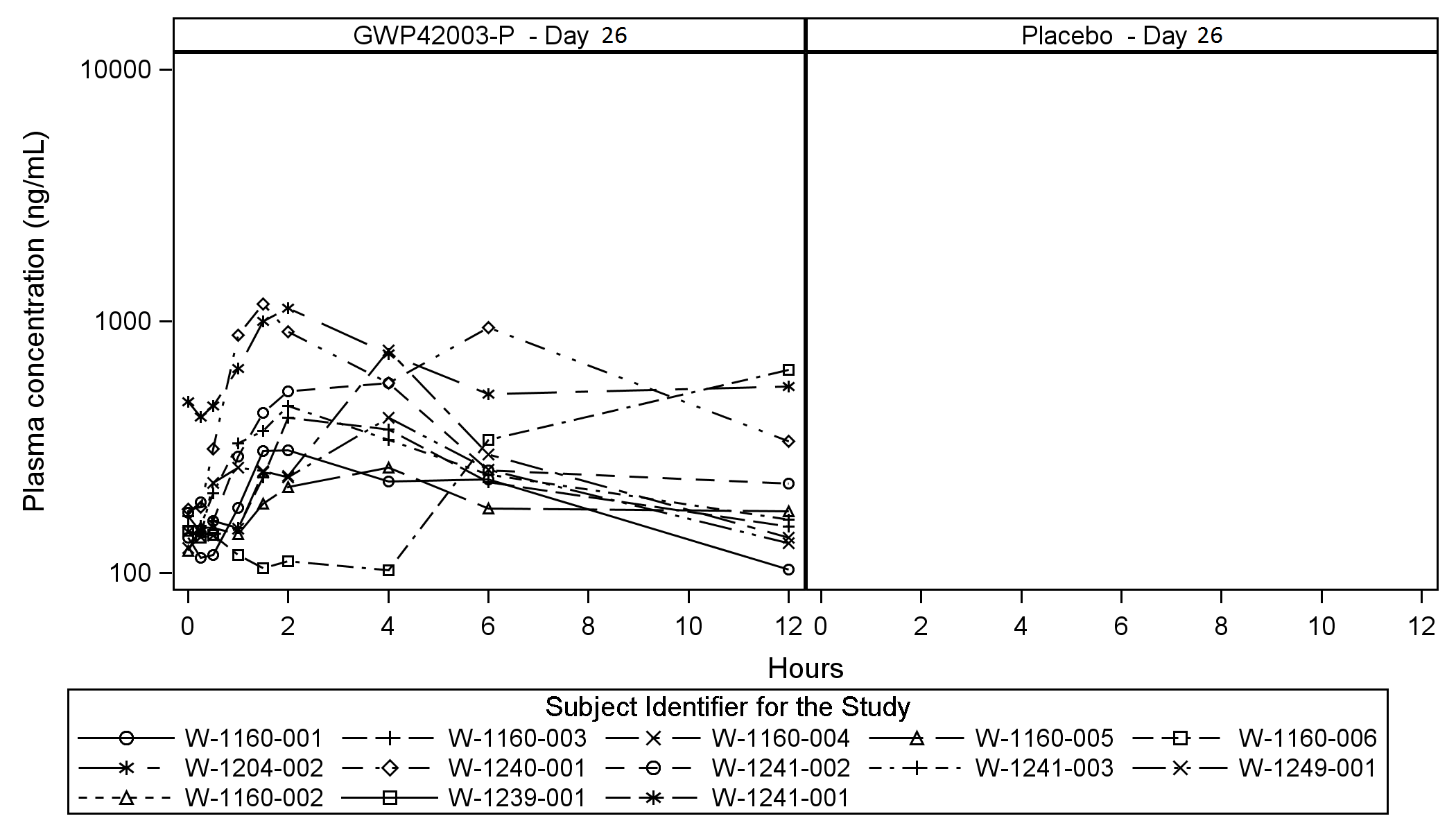
**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.2. PK Indivudual Patient Profile

8.2.7b. Tetrahydrocannabinol - Log10 Scale

PK Population



Source: Listing 8.1

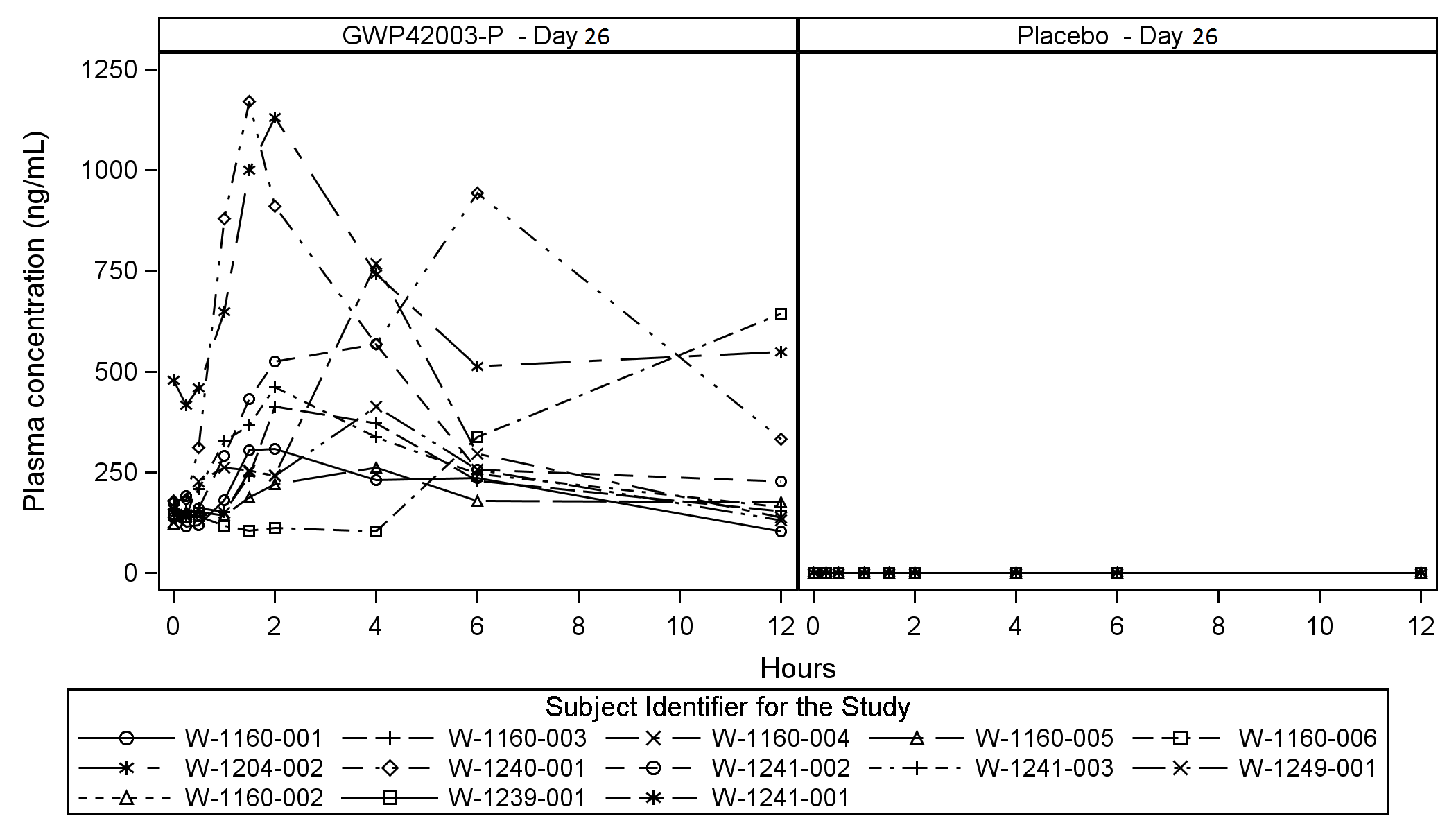
**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.8a. 11-OH Tetrahydrocannabinol

PK Population



Source: Listing 8.1

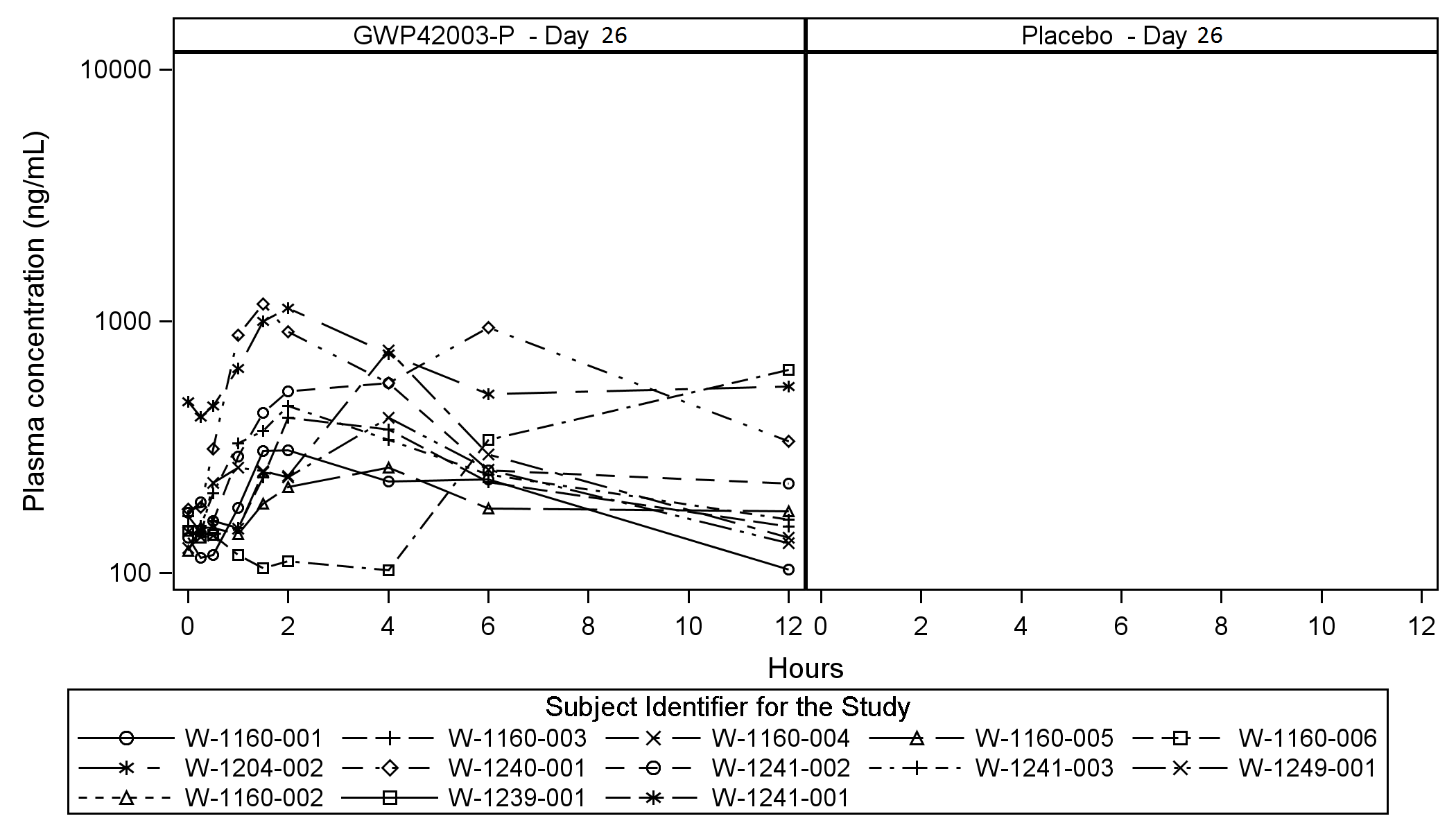
**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.1.8b. 11-OH Tetrahydrocannabinol - Log10 Scale

PK Population



Source: Listing 8.1

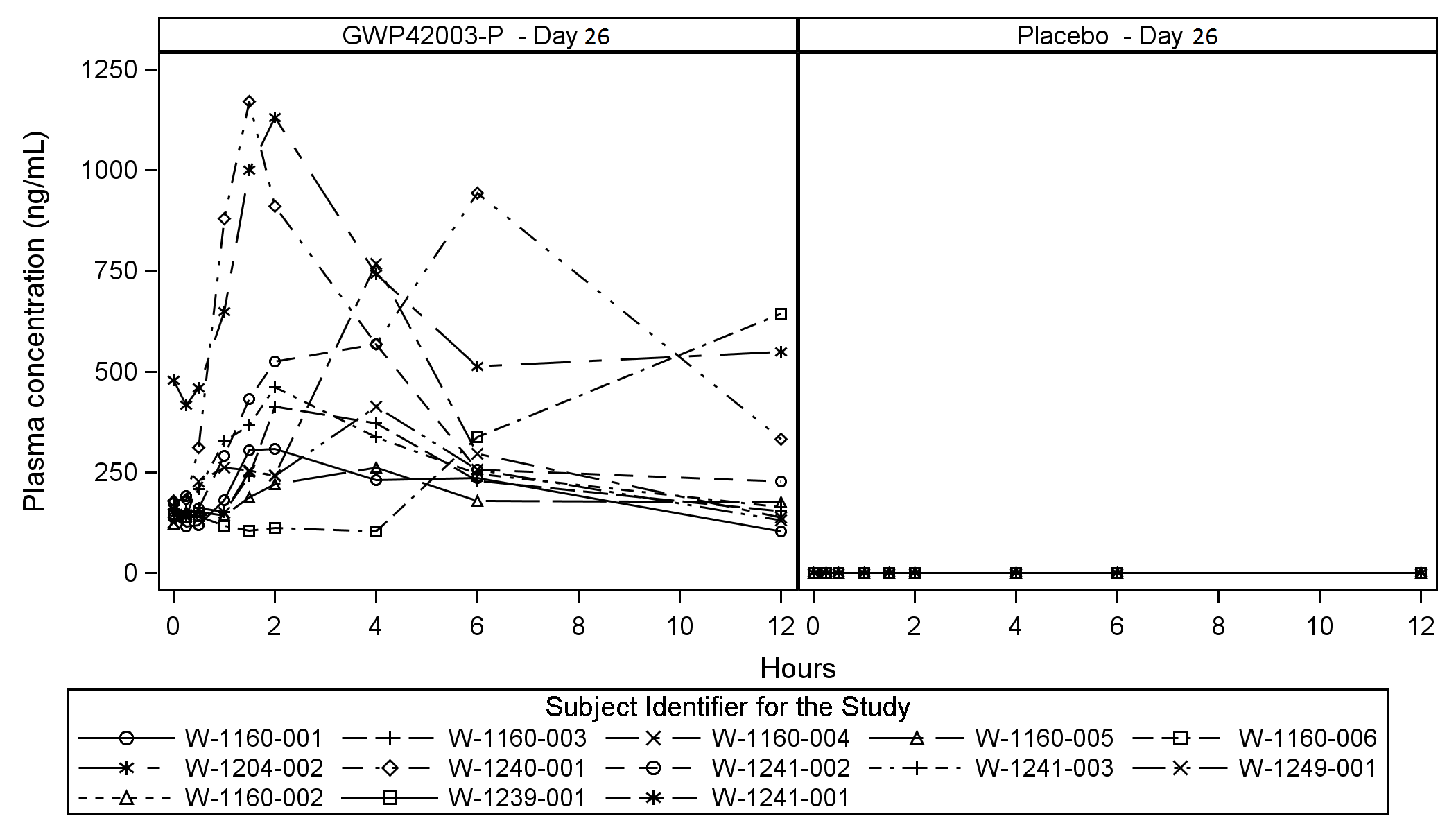
**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.9a. 11-COOH Tetrahydrocannabinol

PK Population



Source: Listing 8.1

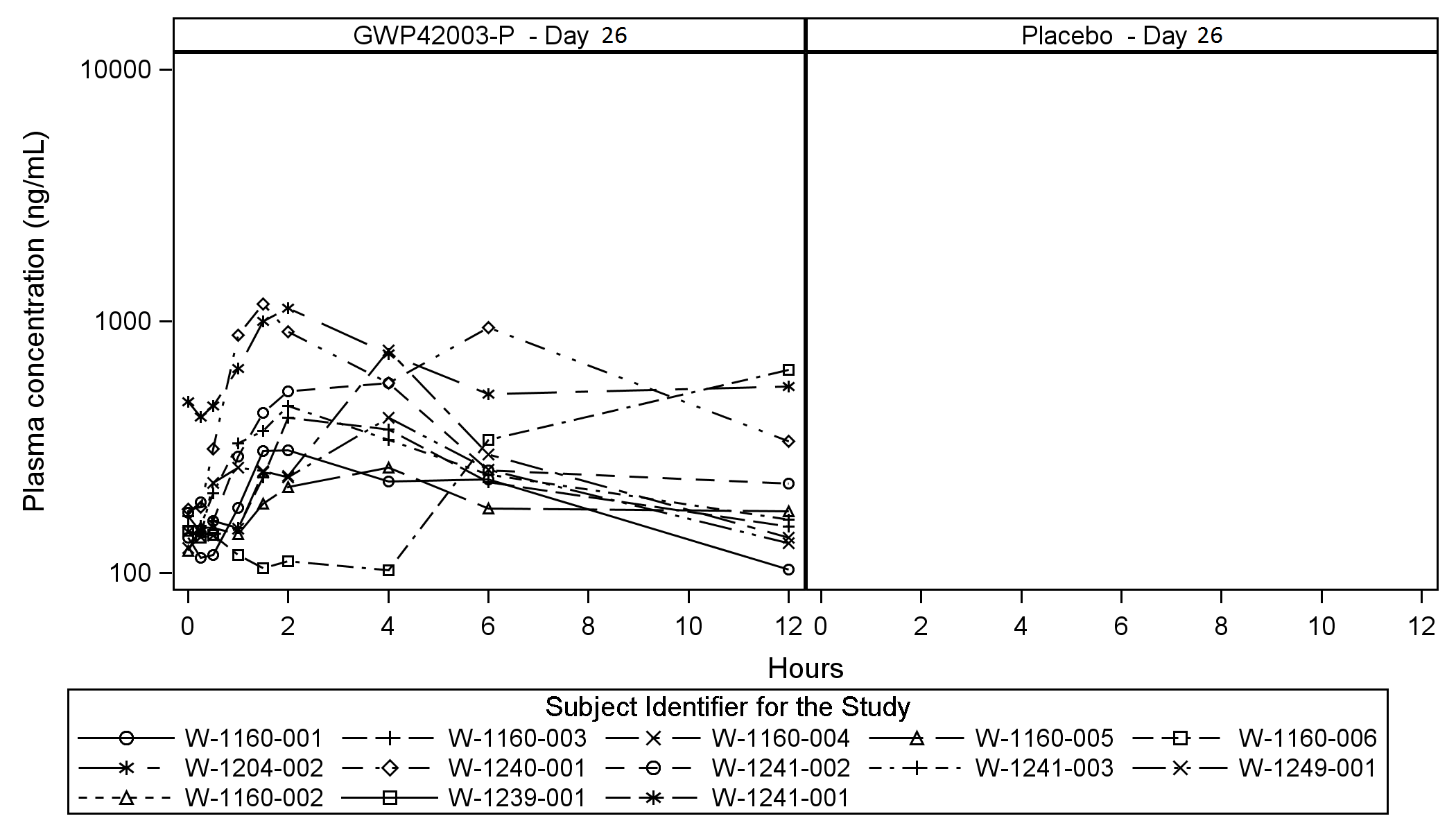
**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.9b. 11-COOH Tetrahydrocannabinol - Log10 Scale

PK Population



Source: Listing 8.1

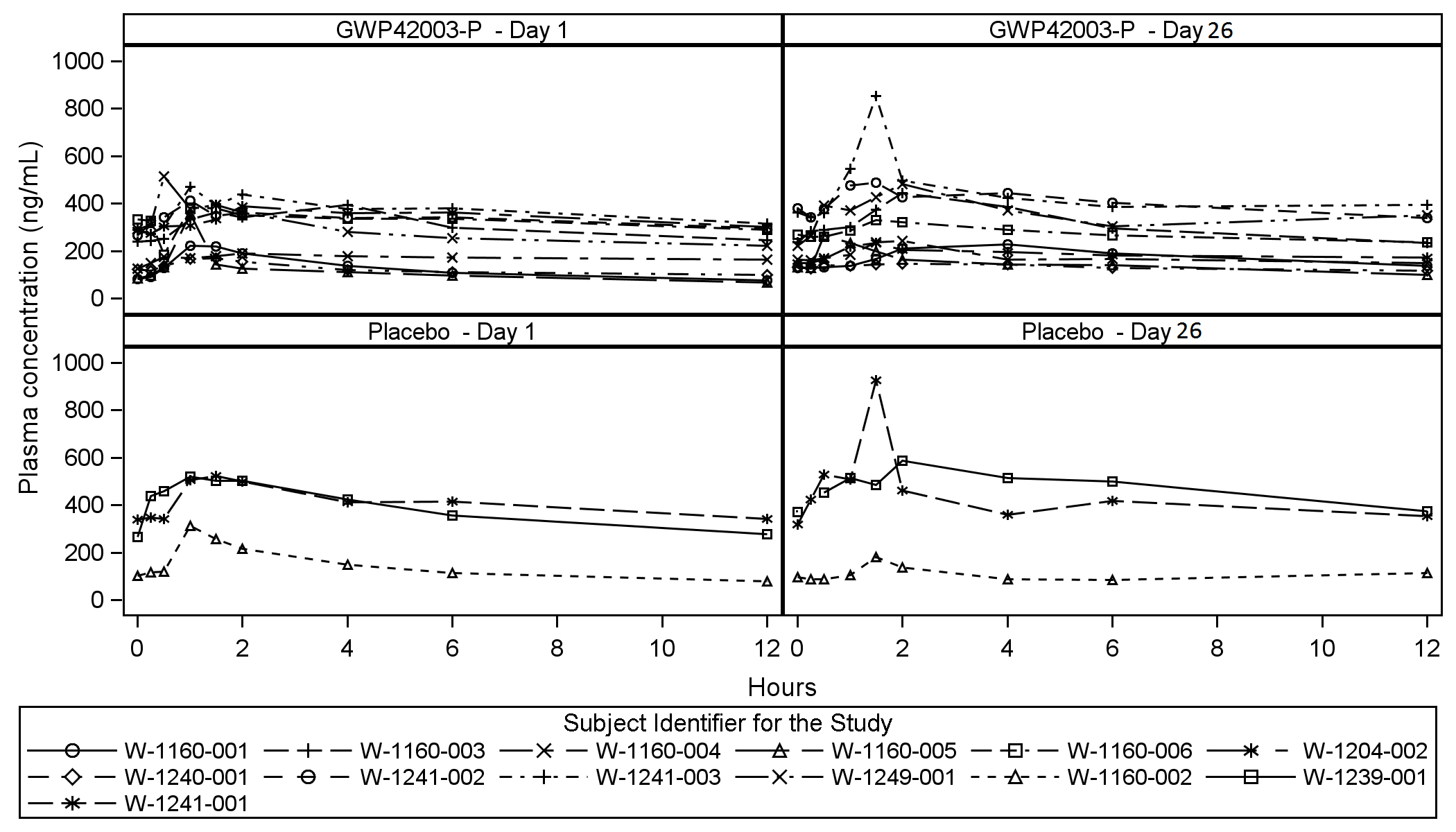
**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.10a. Clobazam

PK Population



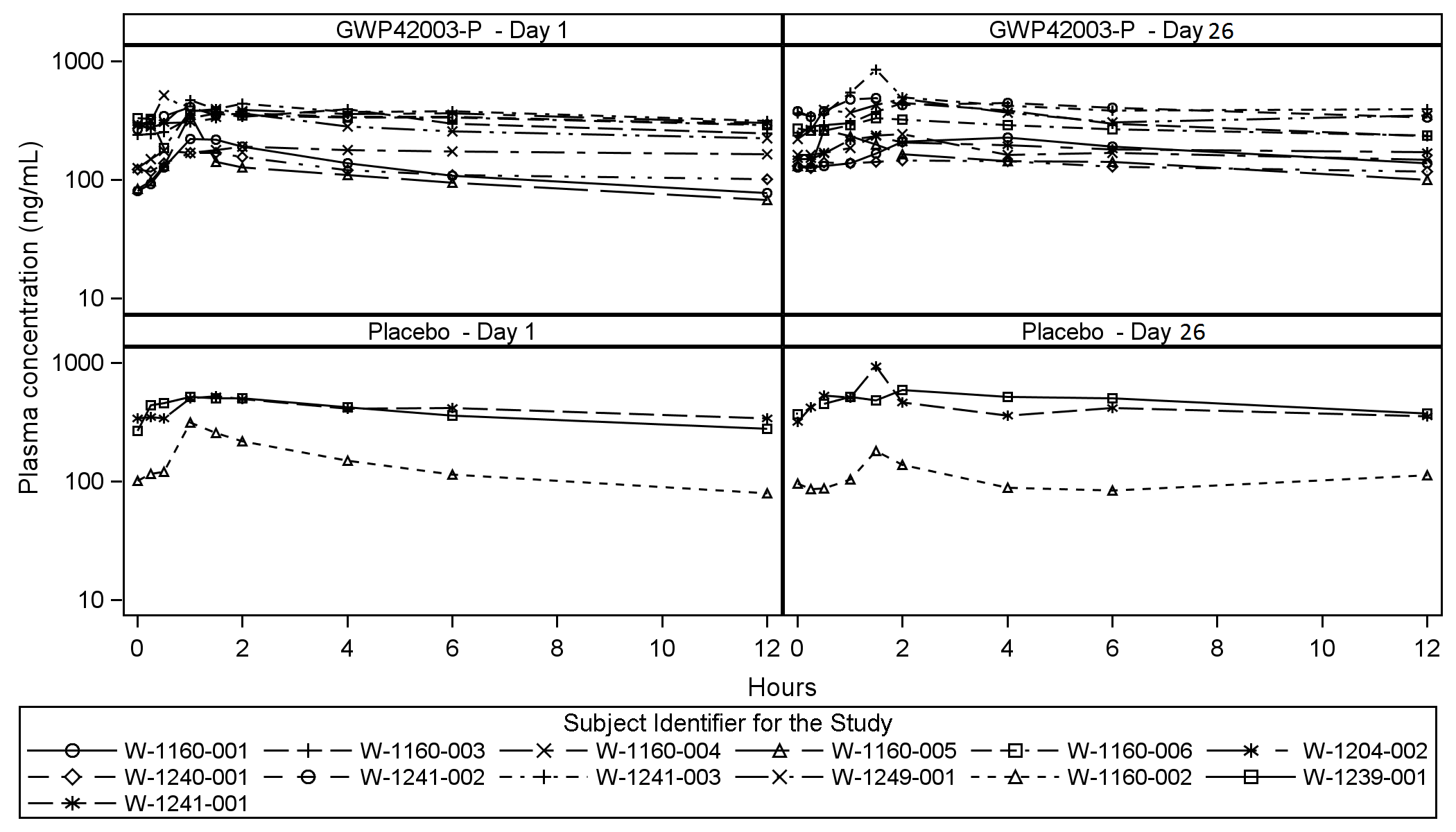
Source: Listing 8.1

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.10b. Clobazam - Log10 Scale

PK Population



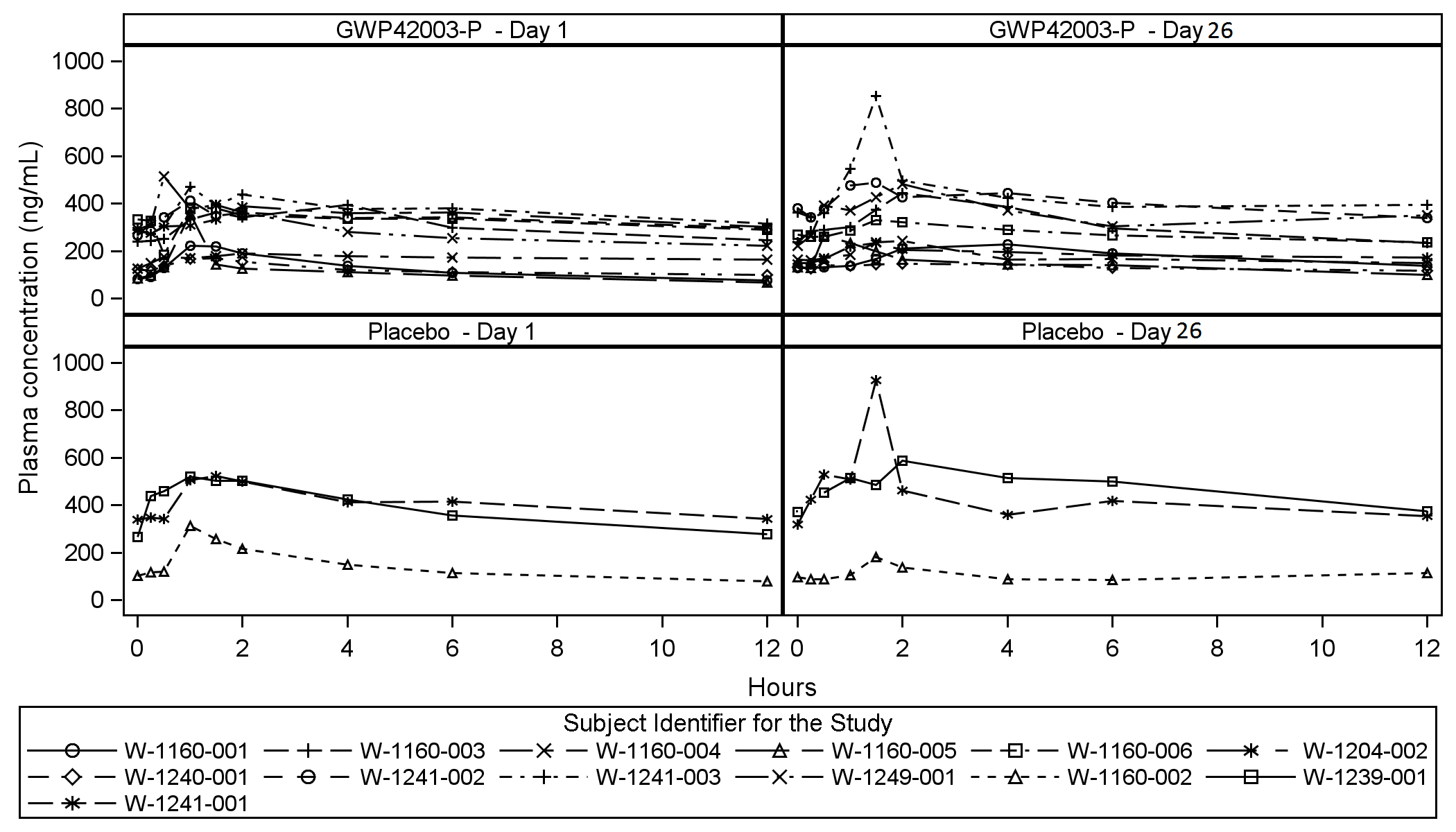
Source: Listing 8.1

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.11a. N-Desmethylclobazam

PK Population



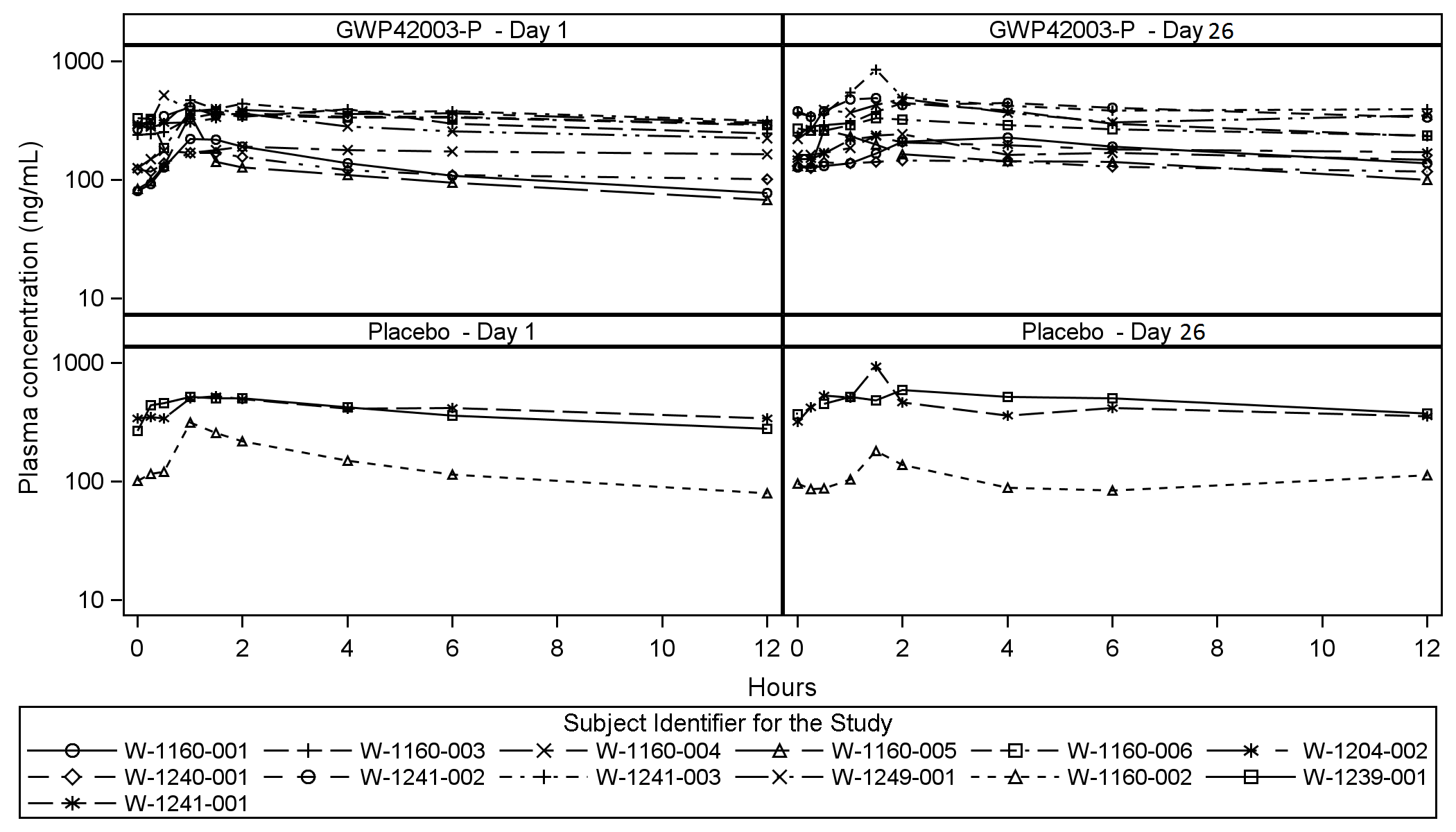
Source: Listing 8.1

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.11b. N-Desmethylclobazam - Log10 Scale

PK Population



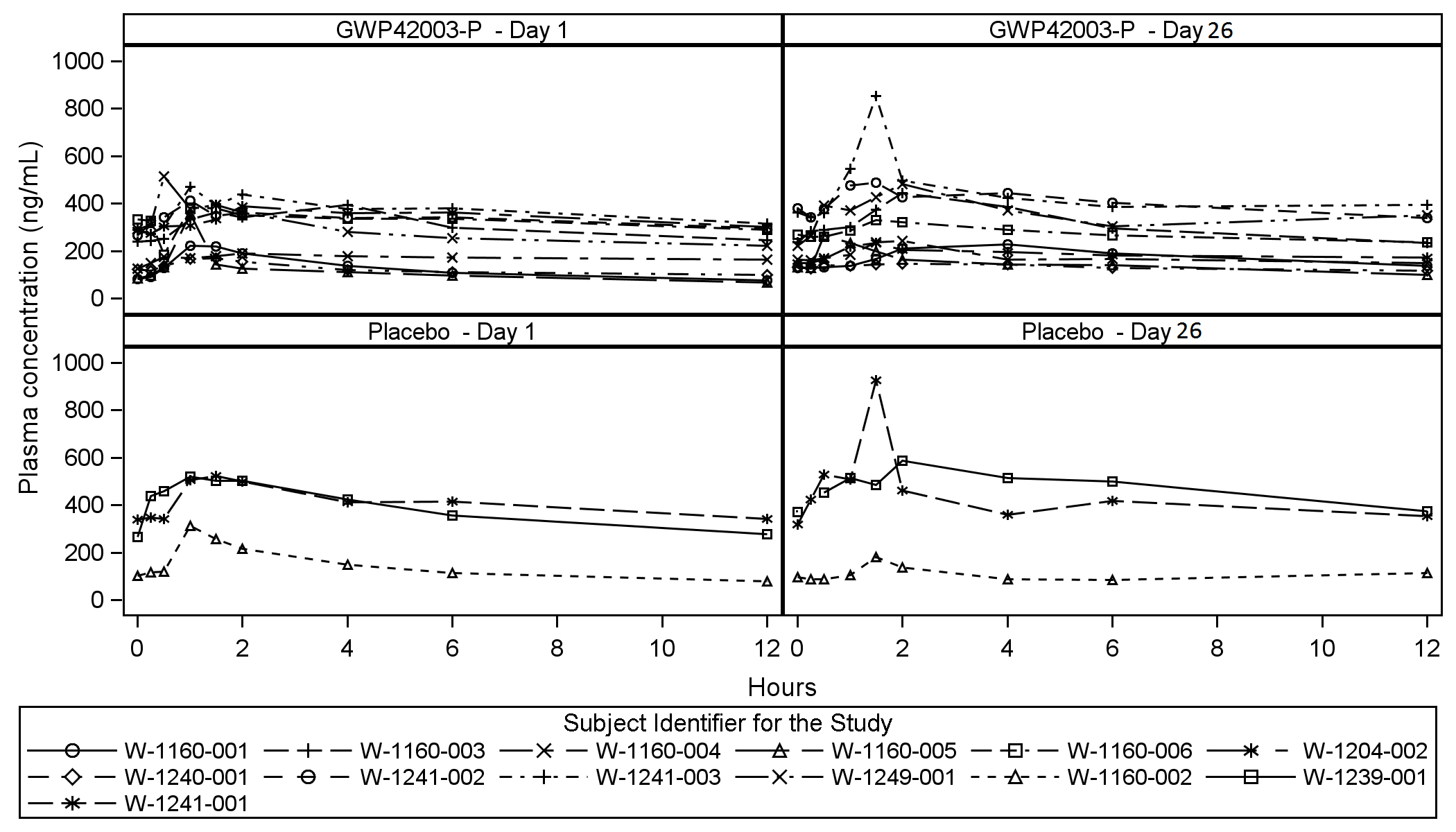
Source: Listing 8.1

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.12a. Levetiracetam

PK Population



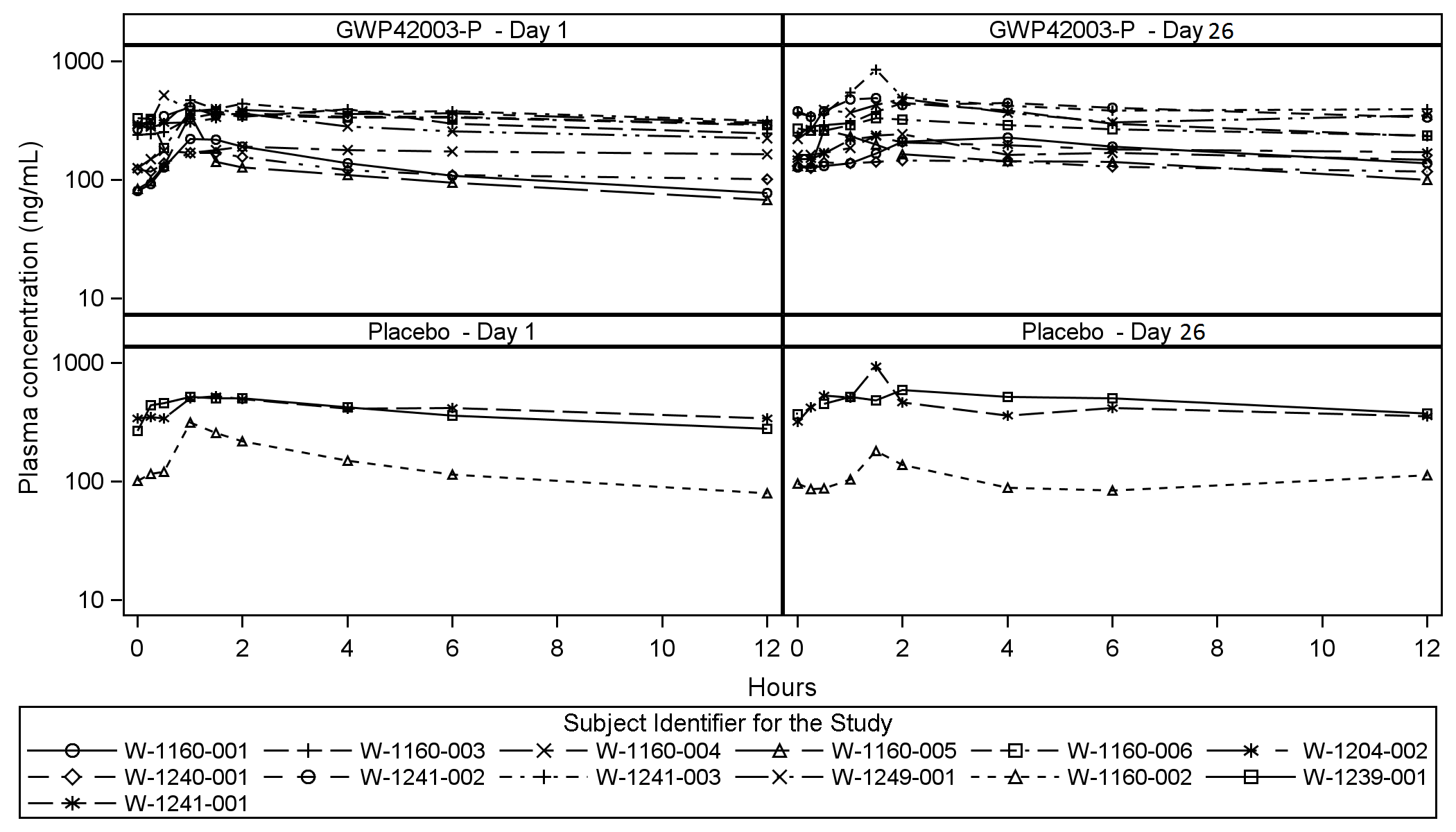
Source: Listing 8.1

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.12b. Levetiracetam - Log10 Scale

PK Population



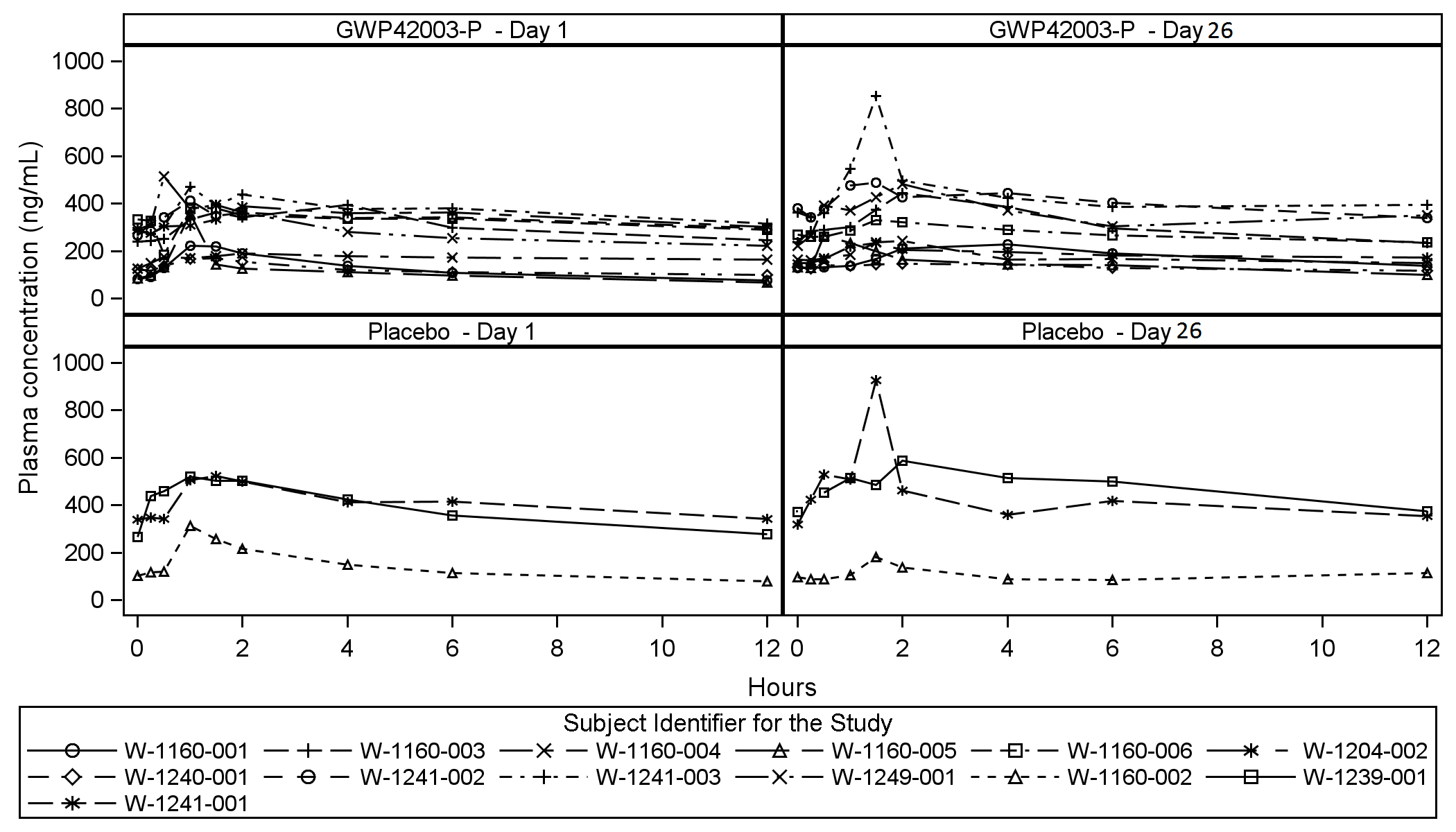
Source: Listing 8.1

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.13a. Topiramate

PK Population



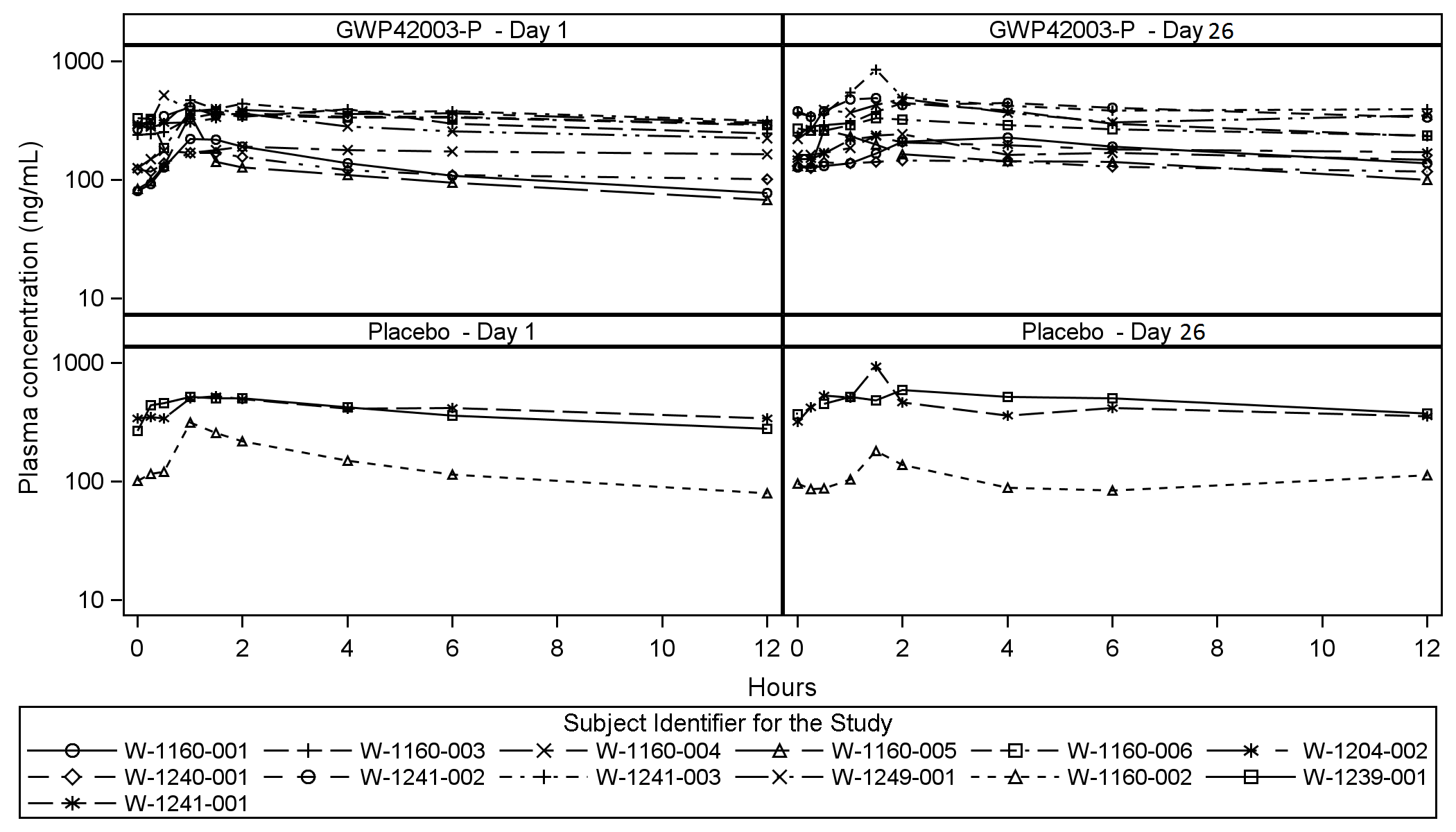
Source: Listing 8.1

8. Pharmacokinetics

8.2. PK Individual Patient Profile

8.2.13b. Topiramate – Log10 Scale

PK Population



Source: Listing 8.1

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.1a. Stiripentol

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

**Programmer’s note:** This title is applicable for STP arm. For VPA arm that will be “8.3.1b. Valproic Acid”.

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.1b. Stiripentol - Log10 Scale

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

**Programmer’s note:** This title is applicable for STP arm. For VPA arm that will be “8.3.1b. Valproic Acid - Log10 Scale”.

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.2a. 4-ene-VPA

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

**Programmer’s note:** Only applicable for VPA arm.

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.2b. 4-ene-VPA - Log10 Scale

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

**Programmer’s note:** Only applicable for VPA arm.

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.3a. Cannabidiol

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.3b. Cannabidiol - Log10 Scale

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.4a. 6-hydroxy cannabidiol

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.4b. 6-hydroxy cannabidiol - Log10 Scale

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.5a. 7-carboxy cannabidiol

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.5b. 7-carboxy cannabidiol - Log10 Scale

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.6a. 7-hydroxy cannabidiol

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.6b. 7-hydroxy cannabidiol - Log10 Scale

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.7a. Tetrahydrocannabinol

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.7b. Tetrahydrocannabinol - Log10 Scale

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.8a. 11-OH Tetrahydrocannabinol

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.8b. 11-OH Tetrahydrocannabinol - Log10 Scale

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.9a. 11-COOH Tetrahydrocannabinol

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.9b. 11-COOH Tetrahydrocannabinol - Log10 Scale

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

**Programmer’s note:** Only Day 26 will be plotted.

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.10a. Clobazam

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.10b. Clobazam - Log10 Scale

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.11a. N-Desmethylclobazam

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.11b. N-Desmethylclobazam - Log10 Scale

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.12a. Levetiracetam

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.12b. Levetiracetam - Log10 Scale

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.13a. Topiramate

PK Population

|  |
| --- |
|  |

Source: Listing 8.1

8. Pharmacokinetics

8.3. PK Individual Patient Profile by Patient

8.3.13b. Topiramate - Log10 Scale

PK Population

|  |
| --- |
|  |

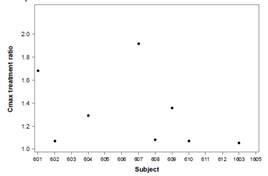
Source: Listing 8.1

8. Pharmacokinetics

8.4. PK Parameters Individual Ratios

8.4.1a. Stiripentol - Cmax

PK Population



Source: Listing 8.2

**Programmer’s note:** This title is applicable for STP arm. For VPA arm that will be “8.4.1a. Valproic Acid - Cmax”.

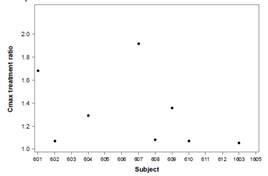
Ratio refers to actual value at Day 26 divided by actual value at Day 1.

8. Pharmacokinetics

8.4. PK Parameters Individual Ratios

8.4.1b. Stiripentol - AUCtau

PK Population



Source: Listing 8.2

**Programmer’s note:** This title is applicable for STP arm. For VPA arm that will be “8.4.1b. Valproic Acid - AUCtau”.

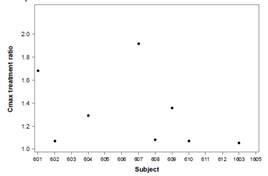
Ratio refers to actual value at Day 26 divided by actual value at Day 1.

8. Pharmacokinetics

8.4. PK Parameters Individual Ratios

8.4.2a. 2-ene-VPA - Cmax

PK Population



Source: Listing 8.2

**Programmer’s note:** Only applicable for VPA arm.

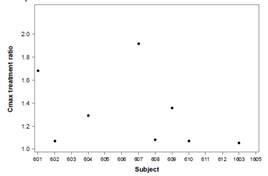
Ratio refers to actual value at Day 26 divided by actual value at Day 1.

8. Pharmacokinetics

8.4. PK Parameters Individual Ratios

8.4.2b. 2-ene-VPA - AUCtau

PK Population



Source: Listing 8.2

**Programmer’s note:** Only applicable for VPA arm.

Ratio refers to actual value at Day 26 divided by actual value at Day 1.

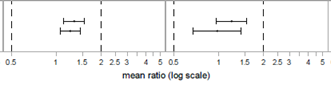
8. Pharmacokinetics

8.5. PK Parameters Mean Ratios

8.5.1a. Stiripentol

PK Population

Cmax AUCtau



Source: Table 8.3.1

**Programmer’s note:** This title is applicable for STP arm. For VPA arm that will be “8.5.1a. Valproic Acid”.

Ratio and 90%CI refer to Day 26 to Day 1 ratio from tables 8.3 Drug Drug Interaction.

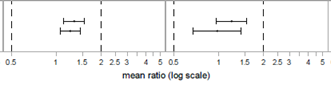
8. Pharmacokinetics

8.5. PK Parameters Mean Ratios

8.5.1b. Stiripentol - Dose Normalized

PK Population

Cmax AUCtau



Source: Table 8.3.2

**Programmer’s note:** This title is applicable for STP arm. For VPA arm that will be “8.5.1a. Valproic Acid - Dose Normalized”.

Ratio and 90%CI refer to Day 26 to Day 1 ratio from tables 8.3 Drug Drug Interaction.

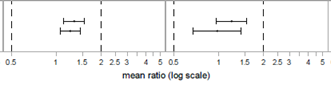
8. Pharmacokinetics

8.5. PK Parameters Mean Ratios

8.5.2a. 2-ene-VPA

PK Population

Cmax AUCtau



Source: Table 8.3.3

**Programmer’s note:** Only applicable for VPA arm.

Ratio and 90%CI refer to Day 26 to Day 1 ratio from tables 8.3 Drug Drug Interaction.

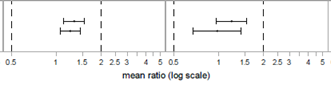
8. Pharmacokinetics

8.5. PK Parameters Mean Ratios

8.5.2b. 2-ene-VPA - Dose Normalized

PK Population

Cmax AUCtau



Source: Table 8.3.4

**Programmer’s note:** Only applicable for VPA arm.

Ratio and 90%CI refer to Day 26 to Day 1 ratio from tables 8.3 Drug Drug Interaction.

**Appendix 2**

**Section A2.1 Demographic Data and Subject Characteristics**

1. Subject Disposition, Visit Attendance, Protocol Violations

1.1. Patient Disposition

Screened Population

| Actual Treatment for DB Phase | Country/ Site | Unique Subject Identifier | Screened | Screen Failure: Reason | Randomized | Date of First Exposure | Date of Last Exposure | End of Treatment Status | Reason for Discontinuation | Specify |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | | | |
| Not randomized | xxxx / xxxx | GWEP1428-W-xxxx-xxx | Y | Y: xxx | N |  |  |  |  |  |
|  | | | | | | | | | | |
| GWP42003-P | xxxx / 1160 | GWEP1428-W-1160-xxx | Y | N | Y | yyyymmdd | yyyymmdd | Completed |  |  |
|  | GWEP1428-W-1160-xxx | Y | N | Y | yyyymmdd | yyyymmdd | Discontinued | Other | xxxxx |
|  |  | … |  |  |  |  |  |  |  |  |
| Placebo | xxxx / xxxx | GWEP1428-W-xxxx-xxx | Y | N | Y | yyyymmdd | yyyymmdd | Completed |  |  |
| GWEP1428-W-xxxx-xxx | Y | N | Y | yyyymmdd | yyyymmdd | Completed |  |  |
|  |  | … |  |  |  |  |  |  |  |  |
| Page 1 of x | | | | | | | | | | |

1. Subject Disposition, Visit Attendance, Protocol Violations

1.2. Inclusion/Exclusion Criteria not Met

Screened Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Visit Name | Criteria | Evaluation |
| --- | --- | --- | --- | --- |
|  | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | PERIOD V1 (D-14) | EXC19 | Unknown |
|  | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | PERIOD V1 (D-14) | INC6 | No |
| … | | | | |
|  | | | | |
| Page 1 of 1 | | | | |

1. Subject Disposition, Visit Attendance, Protocol Violations

1.3. Visit Dates, Including IC Dates

Screened Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Informed Consent | Genetic Testing Informed Consent | V1 (Day -14 to -7) | V2 (Day 1) | V2 (Day 2) | V3 (Day 12) | V4 (Day 33) | V4 (Day 34) |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | | |
| Not randomized | GWEP1428-W-xxxx-xxx | yyyymmdd | --- | yyyymmdd |  |  |  |  |  |
|  | | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd |
|  | GWEP1428-W-xxxx-xxx | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd |
|  | … |  |  |  |  |  |  |  |  |
|  | | | | | | | | | |
| Placebo | GWEP1428-W-xxxx-xxx | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd |
| GWEP1428-W-xxxx-xxx | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd | yyyymmdd |
| … |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
| Page 1 of 1 | | | | | | | | | |

1. Subject Disposition, Visit Attendance, Protocol Violations

1.4. Protocol Deviations

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier\* | Domain | Visit | Type of Deviation\*\* | Description | Importance |
| --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx\* | DB Period | Visit 1 | 4 | xxxxx | Not Important |
|  |  | DB Period | Visit 2 | 6 | xxxxx | Not Important |
|  |  | DB Period | Visit 4 | 5/6 | xxxxx | Important |
| … |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
| \* Excluded from PK population. \*\* 2: Inclusion/Exclusion criteria; 3: Visit date; 4: Patient assessments; 5: Study drug; 6: Labs.                                                                                                                           Page 1 of x | | | | | | |

2. Analysis Sets

Screened Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Screened | Screen Failure | Screen Failure Reason | Safety Population | PK Population | PK Exclusion Reason |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | |
| Not randomized | GWEP1428-W-xxxx-xxx | Y | Y | xxxxxx | N | N |  |
|  | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | Y | N |  | Y | Y |  |
|  | GWEP1428-W-xxxx-xxx | Y | N |  | Y | N | xxxxxx |
|  | … |  |  |  |  |  |  |
|  | | | | | | | |
| Placebo | GWEP1428-W-xxxx-xxx | Y | N |  | Y | Y |  |
|  | GWEP1428-W-xxxx-xxx | Y | N |  | Y | N | xxxxxx |
|  | … |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| PK: Pharmacokinetic.                                                                                                                           Page 1 of 1 | | | | | | | |

3. Demographics

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Date of Birth | Age (years) | Sex | Race | Height (cm) | Weight (kg) | BMI (kg/m2) |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | yyyymmdd | 37.6 | Male | White/Caucasian | 188.0 | 79.8 | 22.6 |
|  | GWEP1428-W-xxxx-xxx | yyyymmdd | 43.2 | Female | Asian | 179.0 | 79.0 | 24.7 |
|  | … |  |  |  |  |  |  |  |
|  | | | | | | | | |
| Placebo | GWEP1428-W-xxxx-xxx | yyyymmdd | 46.5 | Female | White/Caucasian | 161.0 | 69.0 | 26.6 |
|  | GWEP1428-W-xxxx-xxx | yyyymmdd | 45.6 | Male | White/Caucasian | 180.0 | 110.0 | 34.0 |
|  | … |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
| BMI: Body Mass Index.                                                                                                   Page 1 of 1 | | | | | | | | |

4. Baseline Disease Characteristics

4.1. History of Seizures no Longer Occurring

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Seizure Type | Patients Age when This Seizure Type Last Occurred |
| --- | --- | --- | --- |
|  | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | C | 39 years 00 months |
|  | | | |
|  | GWEP1428-W-xxxx-xxx | C | 18 years 00 months |
|  | | | |
|  | … |  |  |
|  | | | |
|  | | | |
| Placebo | GWEP1428-W-xxxx-xxx | C | 25 years 06 months |
|  | | | |
|  | GWEP1428-W-xxxx-xxx | D | 36 years 00 months |
|  | | | |
|  | … |  |  |
| A: Hemiclonic ; B: Complex Partial Seizure (Focal Dyscognitive); C: Secondarily Generalized Tonic Clonic (Evolving to bilateral convulsive Seizure from partial (focal) Seizure); D: Generalized Tonic Clonic Convulsion; E: Absence (any type); F: Myoclonic; G: Tonic; H: Atonic; I: Clonic; J: Tonic/Atonic (cannot differentiate); K: Non Convulsive Status (greater than 30 min); L: Convulsive Status (greater than 30 min); M: Epileptic spasms; N: Other.                                                                                                                  Page 1 of 1 | | | |

4. Baseline Disease Characteristics

4.2. History of Current Seizures

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Seizure Type | Detailed Description of Seizure | Age at Onset of Seizure Type | Seizure Frequency | Seizure Duration | Triggers |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | B | Complex Partial Seizures With Disconnection,oral Automatism | 09 y 00 m | 5 per month | 2-10 mins | Seizure With No Triggers |
|  | C | Secondarily Generalized Seizures With Disconnection. Axial Stiffness Tonic With Convulsive Seizure. | 09 y 00 m | 2 per month | 2-10 mins | Seizure With No Triggers |
|  | | | | | | | |
|  | GWEP1428-W-xxxx-xxx | N | Simple Partial Seizure With Autonomic Systems Or Signs(Epigastric Sensation).) | 39 y | 4 per month | < 2 mins | None |
| Placebo | GWEP1428-W-xxxx-xxx |  |  |  |  |  |  |
| … |  |  |  |  |  |  |  |
|  | | | | | | | |
| A: Hemiclonic ; B: Complex Partial Seizure (Focal Dyscognitive); C: Secondarily Generalized Tonic Clonic (Evolving to bilateral convulsive Seizure from partial (focal) Seizure); D: Generalized Tonic Clonic Convulsion; E: Absence or Atypical absence; F: Myoclonic; G: Tonic; H: Atonic; I: Clonic; J: Tonic/Atonic (cannot differentiate); K: Non Convulsive Status (greater than 30 min); L: Convulsive Status (greater than 30 min); M: Epileptic spasms; N: Other.                                                                                                                             Page 1 of x | | | | | | | |

4. Baseline Disease Characteristics

4.3. Electroencephalography History

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Has the Subject Ever Had an Abnormal EEG | Abnormality 1\* | Abnormality 2\* | Abnormality 3\* | Other, Specify | Seizure Type 1\*\* | Seizure Type 2\*\* | Generalized Specify\*\*\* | Other, Specify |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | Yes | 1 |  |  |  | 1 |  |  |  |
|  | GWEP1428-W-xxxx-xxx | No |  |  |  |  |  |  |  |  |
|  | … | Yes | 6 |  |  |  | 1 |  |  |  |
|  | | | | | | | | | | |
| Placebo | GWEP1428-W-xxxx-xxx | Yes | 1 |  |  |  | 1 |  |  |  |
|  | … |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |
| \* 1: Focal spikes; 2: Generalized spike wave discharges; 3: Hypsarrhythmia; 4: Electrograpic Seizures; 5: Background slowing and/or disorganization; 6: Focal slowing; 7: Other. \*\* 1: Partial (focal) Seizures; 2: Generalized Seizures; 3: Other. \*\*\* 1: Generalized spike & wave; 2: Generalized paroxysmal fast activity; 3: Generalized electrodecrement at onset.                                                                                                                           Page 1 of x | | | | | | | | | | |

4. Baseline Disease Characteristics

4.4. Neuroimaging History

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Has the Patient Had any Neuroimaging Tests Performed in the Past? | Test Number | Date of Test | Method of Imaging | Other, Specify | Result | Abnormality Type | Specify |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | Yes | 1 | 20120222 | MRI |  | Abnormal | Partial | Cortical Dysplasia |
| 2 | 20151009 | MRI |  | Normal |  |  |
|  | | | | | | | | | |
|  | | | | | | | | | |
|  | GWEP1428-W-xxxx-xxx | Yes | 1 | 20120618 | MRI |  | Abnormal | Partial | Mild Right Cerebra Hemiatrophy And Right Mesial Temporal Sclerosis |
|  | | | | | | | | | |
|  | … |  |  |  |  |  |  |  |  |
|  | | | | | | | | | |
| Placebo | GWEP1428-W-xxxx-xxx | Yes | 1 | 20150411 | Other | Brain Pet Fdg | Normal |  |  |
|  | … |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
| Page 1 of x | | | | | | | | | |

4. Baseline Disease Characteristics

4.5. Genetic Testing History

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Has the Patient Had Genetic Testing Performed in the Past? | Test Name | Was a Mutation Found? | Did Either Parent Have the Mutation? | Were They Mosaic for the Mutation? | If Tested Off-site, Has the Report from the Genetic Testing Center Been Received and Filed? | Was a Genome Wide SNP Array Performed? | Was an Epilepsy Gene Panel Performed? | If yes, Spec | Was a Whole Exome Sequencing Performed? |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | No |  |  |  |  | NA |  |  |  |  |
|  | | | | | | | | | | | |
|  | GWEP1428-W-xxxx-xxx | Yes | xxxxx | No | Unknown | Unknown | NA | No | No |  | No |
|  | | | | | | | | | | | |
|  | … |  |  |  |  |  |  |  |  |  |  |
|  | | | | | | | | | | | |
| Placebo | GWEP1428-W-xxxx-xxx | No |  |  |  |  | NA |  |  |  |  |
|  | | | | | | | | | | | |
|  | … |  |  |  |  |  |  |  |  |  |  |
|  | | | | | | | | | | | |
| Page 1 of x | | | | | | | | | | | |

4. Baseline Disease Characteristics

4.6. Previous Use of Cannabis

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Has the Patient Previously Used Cannabis? | Date of Last Use | Time Since Last Use of Cannabis (Months) | If Yes, how Often Did the Patient Use Cannabis? |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | No |  |  |  |
|  | GWEP1428-W-xxxx-xxx | Yes | yyyymmdd | 5 |  |
|  | … |  |  |  |  |
|  | | | | | |
| Placebo | GWEP1428-W-xxxx-xxx | No |  |  |  |
| … |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
| Page 1 of 1 | | | | | |

5. Non-Epilepsy Medical History

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Any Medical History? | System Organ Class | Preferred Term | Condition | Start Date | Stop Date | Status at Screening |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | No |  |  |  |  |  |  |
|  | | | | | | | | |
|  | GWEP1428-W-xxxx-xxx | Yes | Respiratory, Thoracic And Mediastinal Disorders | Asthma | Chronic Asthmatic Bronchitis | 1974 |  | Ongoing |
|  | | | | | | | | |
|  | … |  |  |  |  |  |  |  |
|  | | | | | | | | |
| Placebo | GWEP1428-W-xxxx-xxx | No |  |  |  |  |  |  |
|  | | | | | | | | |
|  | GWEP1428-W-xxxx-xxx | Yes | Psychiatric Disorders | Depression | Mild Depression | 20150807 |  | Ongoing |
|  | | | | | | | | |
| … | | | | | | | | |
|  |  |  |  |  |  |  |  |  |
| Page 1 of x | | | | | | | | |

6. Medications

6.1. History of Antiepileptic Medications and Therapies

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | ATC2 Term | Generic Name | Start Date | End Date | Reason Discontinuation\* | Other, Specify | Comments |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | All Other Therapeutic Products | External Trigeminal Nerve Stimulation | yyyy-mm-dd | yyyy-mm-dd | 1 |  |  |
|  | | | | | | | | |
|  |  | Antiepileptics | Clobazam | yyyy-mm-dd | yyyy-mm-dd | 5 | Change Of Dose |  |
| xxxxxx | yyyy-mm-dd | yyyy-mm-dd | 2 |  |  |
| xxxxxx | yyyy-mm-dd | yyyy-mm-dd | 2 |  |  |
|  | | | | | | | | |
|  | … |  |  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  | | | | | | | | |
| Placebo | GWEP1428-W-xxxx-xxx | Antiepileptics | Carbamazepine | yyyy-mm-dd | yyyy-mm-dd | 5 | Adequate Control |  |
| … |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
| \* 1: Inadequate control; 2: Adverse Events; 3: Epilepsy worsened; 4: Treatment no longer available; 5: Other; 6: Unknown.                                                                                                                            Page 1 of x | | | | | | | | |
|  | | | | | | | | |

6. Medications

6.2. Concomitant AEDs and Dosing

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | AED Name | Time of AM Dose | Time of PM Dose |
| --- | --- | --- | --- | --- |
|  | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | CLOBAZAM | hhmm | hhmm |
|  | hhmm |  |
|  | | | | |
|  | GWEP1428-W-xxxx-xxx | LEVETIRACETAM | hhmm | hhmm |
|  |  |  |
| … |  |  |
|  |  |  |
|  | | | | |
| Placebo | GWEP1428-W-xxxx-xxx | CLOBAZAM | hhmm | hhmm |
| hhmm |  |
| hhmm | hhmm |
| hhmm |  |
|  | | | | |
| … |  |  |  |  |
|  |  |
| Page 1 of x | | | | |

6. Medications

6.3. Other Prior and Concomitant Medications

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Period\* | CM Category | ATC2 Term | Preferred Term | Start/End Date | Dose/Route | Reason Discontinuation | Specify | Indication |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | 1 | HAEM | All Other Therapeutic Products | Other Therapeutic Products | yyyymmdd/ yyyymmdd | xx MG/PO | Inadequate control |  |  |
|  | | | | | | | | | | |
|  |  |  |  | Antiepileptics | Clobazam | yyyymmdd/ yyyymmdd | / | Other |  |  |
|  | | | | | | | | | | |
|  | | | | | | | | | | |
|  |  | 2 | CAEM | Antiepileptics | Carbamazepine | yyyymmdd/ Ong | 400 MG TID /PO |  |  |  |
|  | | | | | | | | | | |
|  | … |  |  |  |  |  |  |  |  |  |
|  | | | | | | | | | | |
| Placebo | GWEP1428-W-xxxx-xxx | 1 | HAEM | Antiepileptics | Carbamazepine | yyyy/ yyyymmdd | / | Inadequate control |  |  |
|  | | | | | | | | | | |
|  | … |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |
| CM: Concomitant Medication; CAEM: Concomitant anti epileptic Medication; HAEM: History of anti epileptic medications and therapies. \* 1: Pre-treatment; 2: Baseline ongoing; 3: DB period emergent.                                                                                                                           Page 1 of x | | | | | | | | | | |

7. Compliance

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Compliance | Visit Name | Visit Date | Did the Patient Comply with the Dosing Schedule? | Does the Actual IMP Usage Reflect the Expected Amount Used as per the Dosing Schedule? | Were There some Signals of Potential Abuse Since Last Visit? |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | Yes | PERIOD V3 (D12) | yyyymmdd | Yes |  |  |
| PERIOD V4 (D26) | yyyymmdd | Yes | Yes | No |
|  | | | | | | | |
|  | GWEP1428-W-xxxx-xxx | No | PERIOD V3 (D12) | yyyymmdd | Yes |  |  |
| PERIOD V4 (D26) | yyyymmdd | Yes | No | No |
|  | … |  |  |  |  |  |  |
|  | | | | | | | |
| Placebo | GWEP1428-W-xxxx-xxx | No | PERIOD V3 (D12) | yyyymmdd | Yes |  |  |
| PERIOD V4 (D26) | yyyymmdd | No | No | No |
|  | | | | | | | |
|  | … |  |  |  |  |  |  |
|  |  |  |  |  |
| Page 1 of x | | | | | | | |

**A.2.2 Efficacy**

**A.2.2.1 Pharmacokinetics Data**

8. Pharmacokinetics

8.1. PK Values

PK Population

| Actual Treatment | Unique Subject Identifier | Parameter (Unit) | Visit | Assessment Date | Time | Analysis Value |
| --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | Clobazam (ng/mL) | Visit 2 Day 1 | yyyymmdd | Pre-dose | 81.0 |
| 15 min | 92.1 |
| 30 min | 128 |
| 1h | 222 |
| 1.5h | 218 |
| 2h | 190 |
| 4h | 139 |
| 6h | 108 |
| 12h | 77.3 |
|  | | | | | | |
|  |  |  | Visit 2 Day 2 | yyyymmdd | 24h | 86.5 |
|  | | | | | | |
|  |  |  | Visit 4 Day 26 | yyyymmdd | Pre-dose | 128 |
| 15 min | 128 |
| 30 min | 131 |
| 1h | 139 |
| 1.5h | 167 |
| 2h | 210 |
| 4h | 228 |
| 6h | 191 |
| 12h | 139 |
| … | | | | | | |
|  | | | | | | |
| 24 hour kinetic data points excluded from PK analysis and plasma concentration-time profiles (12 hour dosing interval).                                                                                                                   Page 1 of x | | | | | | |

8. Pharmacokinetics

8.2. PK Parameters

PK Population

| Actual Treatment | Unique Subject Identifier | Levetiracetam/Stiripentol/Topiramate/Valproate Population Flag | Parameter Category | Visit | Assessment Date | Parameter (Unit) | Analysis Value | Comment |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | N/N/N/N | Clobazam 20 mg/day | Day 1 | yyyymmdd | TMAX (h) | x | xxxxxxxx |
| CMAX (ng/mL) | xxx |  |
| AUCTAU (h\*ng/mL) | xxxx.xx |  |
|  |  |  |  |  |  | … |  |  |
|  | | | | | | | | |
|  |  |  |  | Day 26 | yyyymmdd | TMAX (h) | x.xxx |  |
| CMAX (ng/mL) | xxx |  |
| … |  |  |
|  | | | | | | | | |
|  |  |  | N-Desmethylclobazam 20 mg/day | Day 1 | yyyymmdd | TMAX (h) | x |  |
| CMAX (ng/mL) | xxx |  |
| AUCTAU (h\*ng/mL) | xxxx.xx |  |
|  | | | | | | | | |
| … | | | | | | | | |
|  | | | | | | | | |
| TMAX=Time to the maximum measured plasma concentration; CMAX=Maximum measured plasma concentration; AUCTAU=AUC over a dosing interval; AUCIFO=AUC from zero to infinity obs; AUCIFPE=AUC from zero to infinity with extrapolation of the terminal phase; LAMZHL=Half-life Lambda z; MPAUCR=Metabolite/Parent AUC ratio; MPCMAXR=Metabolite/Parent Cmax ratio.                                                                                                                          Page 1 of x | | | | | | | | |

**A.2.3 Safety**

**A.2.3.1 Exposure to Study Medication**

10. Exposure

10.1. Study Medication

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Treatment Duration (Days) | Visit Name | Date of Administration | Dose Administration on Site?: if no, Reason | Time of Administration (am / pm if Applicable) | IMP Dispensed: number of Packs | IMP Returned: number of Packs | Actual IMP Usage Reflect Expected Amount: if no, Comment | Signals of Potential Abuse |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | xx | PERIOD V2 (D2) | yyyymmdd |  | hhmm | Yes: xx |  |  |  |
|  | | | | | | | | | | |
|  |  |  | PERIOD V4 (D26) | yyyymmdd | No : xxxxx | hhmm/hhmm |  | Yes: x | Yes | No |
|  | | | | | | | | | | |
|  |  |  | PERIOD V4 (D27) | yyyymmdd |  | hhmm | xx |  |  |  |
|  | … |  |  |  |  |  |  |  |  |  |
|  | | | | | | | | | | |
|  | | | | | | | | | | |
| Placebo | GWEP1428-W-xxxx-xxx | xx | PERIOD V2 (D2) | yyyymmdd |  | hhmm | Yes: xx |  |  |  |
|  | | | | | | | | | | |
|  | … |  |  |  |  |  |  |  |  |  |
|  | | | | | | | | | | |
|  | | | | | | | | | | |
|  |  |  |  |  |  |  |  |  |  |  |
| Page 1 of x | | | | | | | | | | |

10. Exposure

10.2. Study Medication Use and Behavior Survey

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Visit Name | Subcategory | Question | Question Result | Question comment |  | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| GWP42003-P | GWEP1428-W-xxxx-xxx | PERIOD V2 (D2) | Desired Use | Addicted to the IMP | Never | xxx |  | |
|  |  |  |  |  |  |  |  | |
|  |  |  | Drug dosage | xxxx |  |  |  | |
| … | | | | | | | |  |
|  |  |  |  |  |  |  |  | |
| Page 1 of x | | | | | | | |  |

10. Exposure

10.3. Study Medication Dose Adjustment

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Date of adjustment | Dose Adjusted | Reason for Dose Adjustment | Adverse Event |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | yyyymmdd | xx MG/KG/DAY | Adverse Event | Diarrhoea |
|  | | | | | |
|  | GWEP1428-W-xxxx-xxx | yyyymmdd | 10 MG/KG/DAY | Adverse Event | xxxx |
| …. | | | | | |
|  |  |  |  |  |  |
| Page 1 of 1 | | | | | |

10. Exposure

10.4. Site Classification Form

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Date of assessment | Categories | Level of Certainty | Relationship to Study Medication |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | yyyymmdd | Misuse | Definite | No |
| GWEP1428-W-xxxx-xxx | yyyymmdd | Therapeutic error | Definite | Unknown/NA |
| … |  |  |  |  |
|  | | | | | |
| Placebo | GWEP1428-W-xxxx-xxx | yyyymmdd | None of the above | Definite | Yes |
| … |  |  |  |  |  |
| Page 1 of 1 | | | | | |

10. Exposure

10.5. Supplemental Drug Accountability

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Date of Assessment | Return of All Drugs: if No, Reason | Specify | Returned Less Than Expected: if Yes, Reason | Specify | Injection Evidence/ Nasal Use | Behavioral Changes/ Suicide Potential | Additional Laboratory Information |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | yyyymmdd | No: xxxx |  | Yes: Other | xxxxx | No / No | No apparent changes / No | No |
| GWEP1428-W-xxxx-xxx | yyyymmdd | Yes |  | No |  | No / No | xxxxx / xx | No |
| … |  |  |  |  |  |  |  |  |
|  | | | | | | | | | |
| Placebo | GWEP1428-W-xxxx-xxx | yyyymmdd | No: Other | xxxx | No |  | No / No | xxxxx / xx | No |
| … |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| Page 1 of 1 | | | | | | | | | |

**A.2.3.2 Adverse Events**

11. Adverse Events

11.1. AEs

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Period | SOC/ PT/ Reported Term\* | Start Date (Day)/ End Date (Day)/ Duration | Serious Event | Severity/ Causality/ Outcome | Action Taken with Study Treatment |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | DB Period | SOC / PT / RT \* | yyyy-mm-dd (xx)/ yyyy-mm-dd (xx)/ xx | N | Severe/ Related / Recovered | Study medication stopped |
|  | | | | | | | |
|  | … |  |  |  |  |  |  |
|  | | | | | | | |
|  | | | | | | | |
| Placebo | GWEP1428-W-xxxx-xxx | DB Period | SOC / PT / RT \* | yyyy-mm-dd (xx)/ yyyy-mm-dd (xx)/ xx | N | Mild/ Not Related / Recovered | None |
| … |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| \* Treatment-emergent AE.                                                                                                                            Page 1 of x | | | | | | | |

11. Adverse Events

11.2. Supplemental AE form

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Assessment Date | Trigger AE | Change in Usage/ Route of Administration | Temporal Relationship/ Other Medications | Frequency/ Consistency | Liking/ Disliking/ Desire to Re-create Event | Intent/ Injection Evidence/ Nasal Use | Behavioral Changes/ Suicide Potential | Additional Laboratory Information |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| GWP42003-P | GWEP1428-W-xxxx-xxx | yyyymmdd | xxxx | xxxx/xxxx | xxxx/xx | xx/xx | x/x/x | xx/x/x | xx/x/x | xxx |
|  |  |  |  |  |  |  |  |  |  |  |
|  | | | | | | | | | | |
|  |  |  |  |  |  |  |  |  |  |  |
| Page 1 of 1 | | | | | | | | | | |

**A.2.3.3 Laboratory Data**

13. Laboratory Evaluations

13.1. Values Overtime

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Category/ Parameter | Analysis Visit | Date and Time (Day) Assessment | Analysis Value | Change/ % Change from Baseline | Indicator (RR) | Toxicity Grade |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | Biochemistry/ Alanine aminotransferase (U/L) | VISIT 1 | yyyymmdd:hh:mm (-x) | xx |  | N [xx-xx] |  |
| VISIT 2 | yyyymmdd:hh:mm (-x) | xx |  | N [xx-xx] |  |
| VISIT 3 | yyyymmdd:hh:mm (xx) | xx | xx/xx.xx | N [xx-xx] |  |
| VISIT 4 | yyyymmdd:hh:mm (xx) | xx | xx/xx.xx | H [xx-xx] | Tox increased |
|  | | | | | | | | |
|  |  | Biochemistry/ Albumin (g/L) | VISIT 1 | yyyymmdd:hh:mm (-x) | xx |  | N [xx-xx] |  |
|  |  | … |  |  |  |  |  |
| … | | | | | | | | |
| RR: Reference Range; N: Normal; H: High; L: Low. \* Baseline value.                                                                                                                          Page 1 of x | | | | | | | | |

13. Laboratory Evaluations

13.3. Clinical Laboratory Blood and Urine Sampling

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Visit Name | Central Laboratory Blood Sample Taken | Urine Sample Taken: Reason | Urine Sample Sent for Central Laboratory/ Result Indicates Medical Condition/ Urine Sample Collected for THC | Repeat Blood Sample: Date | Repeat Urine Sample: Date | Child Bearing Potential: Serum Pregnancy Result | Serum Alcohol Testing: Result | Sample Collected for Genetic Testing |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | PERIOD V1 (D-14) | Yes | Yes | Yes/No/Yes | No | No | NA | Yes: Neg |  |
| PERIOD V2 (D1) | Yes | Yes | xx/xx/xx | No | No |  | Yes: Neg | Yes |
| PERIOD V3 (D12) | Yes | No: xxxx | xx/xx/xx | No | No |  |  |  |
| PERIOD V4 (D26) | Yes | Yes | xx/xx/xx | No | No |  | Yes: Neg |  |
| … |  |  |  |  |  |  |  |  |  |  |
|  | | | | | | | | | | |
| Page 1 of x | | | | | | | | | | |

13. Laboratory Evaluations

13.4. Genetic Testing Data

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Analysis Visit | Date and Time of Assessment | CYP2C19 Result | CYP2C19 Sequence | CYP3A4 Result | CYP3A4 Sequence | Test Level Comment |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | VISIT x | yyyymmdd hh:mm | CYP2C19 \*1/\*1+\*17; Ultrarapid metabolizer | CYP2C19\*1/\*1+\*17 | CYP3A4 \*1/\*1; Extensive metabolizer | CYP3A4\*1/\*1 | xxxxxxxxxx |
|  | GWEP1428-W-xxxx-xxx | VISIT x | yyyymmdd hh:mm | CYP2C19 \*1/\*1 Extensive metabolizer | CYP2C19\*1/\*1 | CYP3A4 \*1/\*1; Extensive metabolizer | CYP3A4\*1/\*1 | xxxxxxxxxx |
| … |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
| Page 1 of x | | | | | | | | |

**A.2.3.4 Vital Signs, Other Physical Findings and Other Safety Data**

14. Vital signs, Other Physical Findings and Other Observations Related to Safety

14.1. Physical Examination and Vital Signs

Safety Population

| Actual Treatment | Unique Subject Identifier | Parameter | Analysis Visit | Date (Day) of Assessment | Analysis Value | Change from Baseline | Percent Change from Baseline | Arm Used |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | Height (cm) | PERIOD V1 (D-14) | yyyymmdd (xx) | xxx\* |  |  |  |
|  | | | | | | | | |
|  |  | Pulse Rate (Beats/min) | PERIOD V1 (D-14) | yyyymmdd (xx) | xx |  |  |  |
| PERIOD V2 (D1) | yyyymmdd (xx) | xx |  |  |  |
| PERIOD V2 (D2) | yyyymmdd (xx) | xx\* |  |  |  |
| PERIOD V3 (D12) | yyyymmdd (xx) | xx | xx | xx.xx |  |
| PERIOD V4 (D26) | yyyymmdd (xx) | xx | xx | xx.xx |  |
| PERIOD V4 (D27) | yyyymmdd (xx) | xx | xx | xx.xx |  |
|  | | | | | | | | |
| Placebo | GWEP1428-W-xxxx-xxx | Sitting Diastolic Blood Pressure (mmHg) | PERIOD V1 (D-14) | yyyymmdd (xx) | xx |  |  | Right |
|  |  | PERIOD V2 (D1) | yyyymmdd (xx) | xx |  |  | Right |
|  |  | PERIOD V2 (D2) | yyyymmdd (xx) | xx\* |  |  | Right |
|  |  | PERIOD V3 (D12) | yyyymmdd (xx) | xx | xx | xx.xx | Right |
|  |  | PERIOD V4 (D26) | yyyymmdd (xx) | xx | xx | xx.xx | Left |
|  |  | PERIOD V4 (D27) | yyyymmdd (xx) | xx | xx | xx.xx | Right |
| … |  |  |  |  |  |  |  |  |
|  | | | | | | | | |
| \* Baseline value.                                                                                                                         Page 1 of x | | | | | | | | |

14. Vital signs, Other Physical Findings and Other Observations Related to Safety

14.2. ECG

Safety Population

| Actual Treatment | Unique Subject Identifier | Parameter | Analysis Visit | Date (Day) of Assessment | Analysis Value | CFB / % CFB | Rhythm: comment | ST or T-wave changes: comment | Infarct pattern/R-wave progression |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | PR Interval (msec) | PERIOD V1 (D-14) | yyyymmdd (xx) | xx |  | Normal | No | No |
| PERIOD V2 (D1) | yyyymmdd (xx) | xx\* |  | Normal | No | No |
| PERIOD V3 (D12) | yyyymmdd (xx) | xx | xx/xx.xx | Normal | No | No |
| PERIOD V4 (D26) | yyyymmdd (xx) | xx | xx/xx.xx | Normal | No | No |
|  | | | | | | | | | |
| … | | | | | | | | | |
|  |  |  |  |  |  |  |  |  |  |
| \* Baseline value. CFB: Change from Baseline.                                                                                                                           Page 1 of x | | | | | | | | | |

14. Vital signs, Other Physical Findings and Other Observations Related to Safety

14.3. Physical Examination, Vital Signs or ECG results indicative of Medical Condition or AE

Safety Population

|  |  |  | Physical Examination Results Indicative of | |  | Vital Signs or Blood Pressure Results Indicative of | |  | ECG Results Indicative of | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Actual Treatment | Unique Subject Identifier | Analysis Visit | a Medical Condition? | an Adverse Event? |  | a Medical Condition? | an Adverse Event? |  | a Medical Condition? | an Adverse Event? |
|  | | | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | PERIOD V1 (D-14) | No |  |  | No |  |  | No |  |
| PERIOD V2 (D1) |  | No |  |  | No |  |  | No |
| PERIOD V2 (D2) |  | No |  |  | No |  |  |  |
| PERIOD V3 (D12) |  | No |  |  | No |  |  | No |
| PERIOD V4 (D26) |  | No |  |  | No |  |  | No |
| PERIOD V4 (D27) |  | No |  |  | No |  |  |  |
| … | | | | | | | | | | |
|  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
| Page 1 of x | | | | | | | | | | |

14. Vital signs, Other Physical Findings and Other Observations Related to Safety

14.4. C-SSRS

Safety Population

| Actual Treatment | Unique Subject Identifier | Parameter | Analysis Visit | Date (Day) of Assessment | Result |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | Wish to be dead | PERIOD V1 (D-14) | yyyymmdd (xx) | No |
| PERIOD V2 (D1) | yyyymmdd (xx) | No |
| PERIOD V3 (D12) | yyyymmdd (xx) | No |
| PERIOD V4 (D26) | yyyymmdd (xx) | No |
|  | | | | | |
|  |  | Non-Specific Active Suicidal Thoughts | PERIOD V1 (D-14) | yyyymmdd (xx) | No |
| PERIOD V2 (D1) | yyyymmdd (xx) | No |
| PERIOD V3 (D12) | yyyymmdd (xx) | No |
| PERIOD V4 (D33) | yyyymmdd (xx) | No |
| … |  |  |  |  |  |
|  | | | | | |
| Page 1 of x | | | | | |

14. Vital signs, Other Physical Findings and Other Observations Related to Safety

14.5. Seizure Data From Patient Diary

Safety Population

| Actual Treatment for DB Phase | Unique Subject Identifier | Visit Name | Date | Nb of Tonic/ Clonic/ Tonic-Clonic/ Atonic/ Myoclonic/ Absence Seizures | Nb of Countable Partial Seizure | Other Partial | No Seizures Today/ Episodes of Status Epilep | AEDs/ Rescue Taken | Study Drug Taken |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | | |
| GWP42003-P | GWEP1428-W-xxxx-xxx | PERIOD V1 (D-14) | yyyymmdd |  | 1 |  | Yes/No | Yes/No |  |
| yyyymmdd |  |  |  | Yes/No | Yes/No |  |
| yyyymmdd |  |  |  | Yes/No | Yes/No |  |
| yyyymmdd |  |  |  | /No | Yes/No | AM/PM |
| yyyymmdd |  |  |  | /No | Yes/No | AM/PM |
| yyyymmdd |  |  |  | /No | Yes/No | AM/PM |
| yyyymmdd |  |  |  | /No | Yes/No |  |
| … |  |  |  |  |  |  |  |  |  |
|  | | | | | | | | | |
| Page 1 of x | | | | | | | | | |