Statistical Analysis Plan

Title: An Open-label, Single-arm Study to Characterize the Pharmacodynamics and Safety of Repeat Dose SP-102 (Dexamethasone Sodium Phosphate Injectable Gel) Administered by Epidural Injection in Subjects with Lumbosacral Radiculopathy

Protocol Number: SP-102-03

Version 1.0

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Author: [redacted]

Previous Versions

SAP Amendments before database lock

Version	Issue Date	Section	Revision/Addition	Rationale

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1 LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

AE	adverse event
AUEC28 days	area under the effect time curve at 28 days post dose
BMI	body mass index
BPI-SF	Brief Pain Inventory-Short Form
bpm	beats per minute
CDISC	Clinical Data Interchange Standards Consortium
CI	confidence interval
ECG	electrocardiogram
Emax	maximum effect
EOS	end of study
ET	early termination
HbA1c	Hemoglobin A1c
HIV	human immunodeficiency virus
MedDRA	Medical Dictionary for Regulatory Activities
mg	milligram
MRI	magnetic resonance imaging
NPRS	Numeric Pain Rating Scale
PD	pharmacodynamic
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
T1	Treatment 1 – Index injection
T2	Treatment 2 - Repeat injection
TF	transforaminal
WBC	white blood cells

2 INTRODUCTION

This document details the planned statistical analyses for the Semnur Pharmaceuticals, Inc, protocol "SP-102-03" study titled "An Open-label, Single-arm Study to Characterize the Pharmacodynamics and Safety of Repeat Dose SP-102 (Dexamethasone Sodium Phosphate Injectable Gel) Administered by Epidural Injection in Subjects with Lumbosacral Radiculopathy."

The proposed analyses are based on the contents of the final version of the protocol (dated 08-JUN-2018).

This is an open-label, single-arm, repeat dose study to characterize the PD and safety/tolerability of SP-102 (10 mg dexamethasone) administered by epidural injection as transforaminal (TF) or interlaminar (IL) injection under fluoroscopic guidance in subjects with lumbosacral radiculopathy.

Subjects meeting the eligibility criteria will be enrolled in the study and receive a single 2-mL epidural injection of SP-102 (10 mg dexamethasone) in T1 (index injection) and T2 (repeat injection), separated by 4 to 8 weeks. T2 will only be provided if a repeat injection is warranted and the subject continues to meet applicable study inclusion and exclusion criteria.

3 STUDY OBJECTIVES

3.1 Primary Objective

The primary objective of the study is to characterize repeat dose pharmacodynamics (PD) of SP-102 (10 mg dexamethasone) administered by epidural injection with respect to hypothalamic-pituitary-adrenal (HPA) suppression using plasma cortisol levels, white blood cell count (WBC), and blood glucose.

3.2 Secondary Objective

The secondary objectives of the study are to:

- Evaluate the safety and tolerability of single and repeat dose SP-102 (10 mg dexamethasone) administered by epidural injection in subjects with lumbosacral radiculopathy.

- Evaluate the analgesic effect on leg pain (as measured by the Numeric Pain Rating Scale [NPRS] in the affected leg) following the index (Treatment [T1]) and repeat (T2) injections.

4 ENDPOINTS

4.1 Pharmacodynamic Endpoints

- Dexamethasone-induced HPA suppression as measured by:
  - Observed total blood cortisol levels, change from baseline cortisol levels, and percent change from baseline cortisol levels
  - Observed glucose levels, change from baseline glucose levels, and percent change from baseline glucose levels
  - Observed white blood cell counts, change from baseline white blood cell counts, and percent change from baseline white blood cell counts

- NPRS (average leg pain and back pain) and BPI-SF
- Change from T1 Day 0 and T2 Day 0 through Day 28 in NPRS (average leg pain and back pain) and BPI-SF over time following the index (T1) and repeat (T2) epidural injections, respectively
- Percent change from T1 Day 0 and T2 Day 0 through Day 28 in NPRS (average leg pain and back pain) and BPI-SF following the index (T1) and repeat (T2) epidural injections, respectively

4.2 Safety Endpoints

- Incidence of treatment-emergent AEs (TEAEs) and serious adverse events (SAEs)
- Change from baseline in clinical laboratory parameters, vital sign measurements, ECG findings, physical examination, general neurological examination findings, and targeted neurological examination parameters following each treatment.

5 SAMPLE SIZE

No formal statistical power calculation was performed for this study; the sample size is based on clinical and practical considerations. Enrollment will continue until 12 subjects have each completed two SP-102 injections (T1 and T2).

6 RANDOMIZATION

This is an open-label study; there is no blinding. All subjects will receive SP-102 for each of the injections.

7 PLANNED ANALYSES

No statistical analysis plan (SAP) prepared in advance of the data can be absolutely definitive and the final clinical study report (CSR) may contain additional tables or statistical tests if warranted by the data obtained. The justification for any such additional analyses will be fully documented in the final CSR.

7.1 Analysis Sets

Subjects excluded from the analysis sets and the reason for their exclusion will be listed in Appendix 16.2.

7.1.1 Screened Population

This consist of subjects who signed the ICF and are assigned a study subject number.

7.1.2 Safety Analysis Population

The Safety Analysis population is defined as all enrolled subjects who receive at least one SP-102 injection.

7.1.3 PD Analysis Population

The PD Analysis population is defined as all enrolled subjects who have a T1 period baseline PD result and at least 1 post-dose PD assessment result without any protocol deviations available in either T1 or T2.

Major protocol violations that impact the PD analysis may lead to exclusion from the PD population.

7.1.4 Complete Analysis Population

The Complete Analysis population is defined as all enrolled subjects who receive only one SP-102 injection who complete T1 – Day 28 plus those subjects who receive two SP-102 injections who complete T2 – Day 28.

7.2 Baseline

Unless otherwise specified, baseline is defined as the last non-missing measurement taken prior to treatments T1 or T2 (reference start date). This includes screening or unscheduled assessments that would have been performed no earlier than 21 days before the reference start date.

In the case where the last non-missing measurement and the reference start date coincide, that measurement will be considered pre-reference, but AEs and medications commencing on the reference start date will be considered post-reference.

For laboratory tests, baseline is defined as the last measurement obtained during screening prior to T1.

For vital signs parameters, an assessment performed on reference start date with time point marked as "pre-dose" will be considered as baseline for the given treatment period.

Baseline ECG is the last measurement prior to the index injection.

For physical exams, baseline is defined as the last assessment prior to T1 on Day 0.

For General and Targeted Neurological Exam baseline for each treatment period is defined as the pre-dose assessment.

For cortisol suppression, glucose, and white blood cell counts, baseline is defined as the last non-missing value obtained prior to T1 or T2, which is T1/T2 Day 1 pre-dose measurement.

For NPRS and BPI-SF, baseline is defined as the last non-missing value obtained prior to T1 or T2, which is T1/T2 Day 0 measurement.

7.2.1 Duration/Study Day/Time

There are two reference start dates, one for the index injection and one for the repeat injection. Study day will appear in every listing where an assessment date or event date appears.

Study Day for assessments during the treatment period will be calculated for each treatment period using the dosing day for each period as the reference start date (that is, days during the T1 period should be calculated from Index dosing time, and days during T2 period should be calculated from repeat dosing time) and will be used to show start/stop day of assessments and events.

- Therefore, if the date of the assessment/event is on or after the reference date then:

  Study Day = (date of assessment/event – reference date) + 1.

  Study day for assessments prior to start of treatment will use the index injection date as the reference date.

- Therefore, if the date of the assessment/event is prior to the reference date then:

  Study Day = (date of assessment/event – reference date).

7.2.2 Conventions for Missing and Partial Dates

All rules explained below for partial/missing dates will be followed unless contradicted by any other data recorded on the electronic Case Report Form (eCRF).

All dates presented in the individual subject listings will be as recorded on the eCRF (i.e., not completed as per the below rules).

7.2.3 Missing/Partial Start/Stop Date of Adverse Events and Concomitant Medications

Missing and partial start and stop date will be imputed for analysis purposes as follows

Partial or missing stop date will be imputed as follows:

If the stop date is completely missing and the event has resolved or the subject has stopped taking the concomitant medication, the stop date will be imputed as the date of the subject's last clinic visit in the study.

- If only the year is known, the stop date will be imputed as "31-Dec" of that year or as the date of the subject's last clinic visit in the study if in the same year.
- If the month and year are known, the stop date will be imputed as the last day of that month unless the stop date corresponds to the same month as the subject's last clinic visit in which case the date of subject's last clinic visit in the study will be used instead.

Missing start date will be imputed as follows:

- If the stop date occurs on or after the start of study drug or the event/concomitant medication is ongoing, the start date will be imputed as the date of the first dose of study drug.
- If the stop date occurs before the start of study drug, the start date of the event/concomitant medication will be imputed as the subject's screening date or the stop date of the event/concomitant medication whichever the earlier.

Partial start date (year present, but month and day missing)

- If the stop date occurs on or after the start of study drug or the event/concomitant medication is ongoing, and the year is the same as the year of first dosing the start date will be imputed as "01-Jan" of the same year or the date of the first dose of study drug

whichever is latest. If the year is different from the year of first dosing "01-Jan" will be used.

- If the stop date occurs before the start of study drug, the start date of the event/concomitant medication will be imputed as the "01-Jan" of the same year.

Partial start date (month and year present, but day missing)

- If the stop date occurs on or after the start of study drug or the event/concomitant medication is ongoing, the start date will be imputed as the first day of the same month and year unless this partial start date is in same month as the first dose of study drug in which case the date of first dose of study drug will be used.
- If the stop date occurs before the start of study drug, the start date will be imputed as the first day of the month and year of the partial stop date.

7.2.4 Electrocardiogram Data

For ECG data recorded on continuous scales, if more than one value is recorded at a time point, the mean value rounded to the integer will be presented. For overall interpretation if more than one value is recorded, the most severe (worst case) of the respective readings will be taken.

7.2.5 Unscheduled Visits

Except for ET assessments, only scheduled post-baseline laboratory and vital signs values will be tabulated. Post-baseline repeat/unscheduled assessments will be disregarded, although these post-baseline assessments will be listed in the relevant appendices to the CSR.

For post-baseline PD, laboratory and vital sign data, if an Early Termination assessment falls between two visits and the visit prior to that ET visit has a valid assessment, then that ET assessment will be mapped to the subsequent visit within the treatment period. If the scheduled assessment prior to an ET assessment is missing, then the ET assessment will be mapped to that prior assessment. Assessments from T1 cannot be assigned to T2.

7.3 Conventions

All data listings, summaries, figures and statistical analyses will be generated using SAS version 9.4 or higher[1].

Summaries will be presented by treatment (Treatment 1 and 2). Treatment periods (T1/T2) will be displayed as follows:

Treatment 1	Treatment 2	Overall

Overall columns are to be included within the table shells as follows:

Demography	Overall
Baseline	Overall
Disposition	Overall
PD	Treatment
AEs	Treatment & overall
Other safety	Treatment

Listings will be sorted in the following order subject, treatment period (T1/T2), parameter, and study day unless otherwise stated.

Continuous variables will be summarized by the number of non-missing observations, mean, median, standard deviation, and minimum and maximum.

Categorical variables will be summarized by presenting the frequency and percent. Percentages will be based on the number of non-missing observations or the subject population unless otherwise specified. For each variable, all categories will be shown. Zero frequencies (but not the percent) within a category will be presented.

7.3.1 Decimal Places

Decimal places for derived data will be determined by the scale of measurement unless otherwise stated. No decimal places will be displayed if the smallest calculated value is ≥ 100; 1 decimal place will be displayed when the smallest value is within the interval (10, 100), with 10 being inclusive; 2 decimal places will be displayed when the smallest value is within (1, 10), with 1 being inclusive; and so on for even smaller scales of measurement.

Derived data where it is known in advance the result will be an integer for example day, month, year, number of days and total scores (for rating scales) will be presented with zero decimal places.

Means, medians and percentiles will be displayed to one more decimal place than the data**,** dispersion statistics (e.g. standard deviation) will have two more decimal places, and the minimum and maximum will be displayed to the same number of decimal places as reported in the raw data. Percentages will be displayed with one decimal place.

P- Values will be quoted to 3 decimal places. P-values < 0.001 will be presented as p<0.001. Where this value is less than 0.05, 0.01 or 0.001, attention will be drawn to this fact using the conventional "*", "**" or "***" annotation, respectively.

7.4 Derived Variables

7.4.1 Area under the effect curve over 28 days (AUEC28)

AUEC28 days is defined as the change from baseline (for cortisol, glucose, and WBC) and calculated using linear trapezoidal summation from pre-dose to Day 28 in each treatment period.

AUEC28 analyses for the for cortisol, glucose, and WBC will be based on the assumption that the baseline assessment take place at time zero. Only scheduled and ET visit assessments will be included in the computation. If the actual time is not recorded the nominal time will be used. Cortisol, glucose, and WBC ET assessments will be mapped to Day 28 and AUEC28 will then be computed.

If a subject has no pre-dose value, AUEC28 will not be calculated. In the case where a subject has two values recorded at the same time, the two scores will be averaged.

7.4.2 Maximum Effect (Emax)

Emax is the maximum increase from baseline (pre-treatment level, T1 or T2) in glucose level and WBC count or the maximum decrease in cortisol levels over the 28 days post dose in each treatment period. An Emax value will be calculated for cortisol, glucose, and WBC for each treatment period (T1/T2).

7.4.3 BPI-SF variables

Pain Severity Score = Mean of items 3-6 (pain at its worst, pain at its least, average).

Pain Interference Score = Mean of items 9A-9G (interference of pain with: general activity, mood, walking, normal work, relations, sleep, enjoyment of life)

7.5 Subject Disposition

Subject disposition will be summarized as follows:

- The number of subjects that were screened, number that failed screening, and number in each analysis set will be summarized by treatment period and overall using the Screened Population.

- The number of early discontinuations and the reasons for withdrawals will be summarized by treatment period (T1/T2) and overall (T1 and T2) for the Safety Analysis population.
- The number of subjects who complete each treatment period of the study and the number of subjects present at each scheduled visit will be summarized by treatment period for the Safety Analysis population.

7.6 Protocol Deviations

Protocol deviations will be adjudicated into major and minor. A listing of both major and minor protocol deviations will be provided.

7.7 Baseline Comparability

Demographics and baseline characteristics will be assessed in a descriptive manner, and no formal statistical testing will be performed.

Standard continuous or categorical variable summaries will be presented for all subjects for the following variables based on the Safety Analysis population.

7.8 Demographic data

The following demographic variables will be summarized for all subjects: Age (years), gender, childbearing potential, race, ethnicity, height (cm), weight (kg), BMI (kg/m^2), Straight leg raise, Femoral stretch test, Hepatitis B Surface Antigen, Hepatitis C Virus Antibodies, HIV-1 Antibody, and HIV-2 Antibody.

7.9 Medical History

Summaries of previous and ongoing conditions at screening will be presented. Conditions will be presented by Medical Dictionary of Regulated Activities (MedDRA) primary system organ class and preferred term.

7.10 Prior and Concomitant Medications

Prior medications are defined as all medications starting and ending before the first dose of study drug. Prior medications will be summarized for all subjects. Concomitant medications are defined as medications taken on or after the date of the index injection through the EOS/ET participation. Concomitant medications will be summarized by treatment period (T1/T2) using ATC Level 2 and listed. If the onset date of a concomitant medication is on or post the index injection dosing date but before the repeat injection dosing date, it will be considered as occurring during T1; otherwise,

the onset date of concomitant medication on or post the repeat injection date will be considered as occurring in T2. If a medication is taken during both treatment periods it will be counted in both periods.

7.11 Pharmacodynamic Analyses

All comparisons between treatments will be analyzed in log scale but will be reported as ratios with 90% confidence intervals for the difference. All PD analyses will use the PD Analysis population as the primary analysis population.

7.11.1 Dexamethasone-induced HPA suppression

Blood samples for PD will be collected at screening, for T1 at pre-dose (baseline), Days 1, 2, 3, 4, 5, 8, 15, and 28, for T2 at pre-dose (baseline), Days 1, 2, 3, 4, 5, 8, 15 and 28.

Dexamethasone-induced HPA suppression will be evaluated by using the observed plasma cortisol level, blood glucose levels, and WBC count. Plasma cortisol levels, plasma WBC counts, and fasting plasma blood glucose levels will be summarized by treatment group and day using descriptive statistics for observed, change from baseline, and percent change from baseline values. Summary tables will include, the arithmetic mean, standard deviation, coefficient of variation, minimum, maximum, median, and geometric means will also be reported.

7.11.2 NPRS

NPRS assessments will be done at screening, for T1 at Days 0 (baseline), 1, 2, 3, 4, 5, 8, 15, and 28. For T2, NPRS will be done at Days 0 (baseline), 1, 2, 3, 4, 5, 8, 15, and 28. Baseline for each treatment period is the NPRS score taken before the injection on Day 0.

The NPRS is an 11-point scale (0 to 10-point scale where 0 is no pain and 10 is worst pain imaginable) that allows the subject to rate the severity of their pain intensity at various points in time. The subject will use the NPRS to record their current pain, average pain in the past 24 hours, and worst pain in the past 24 hours for both their affected leg(s) and back pain. The NPRS assessments will be summarized by treatment period and day using descriptive statistics for observed, change from baseline, and percent change from baseline values.

7.11.3 BPI-SF

BPI-SF will be collected for T1 at Days 0 (baseline), 1, 2, 3, 4, 5, 8, 9, and 10. For T2, NPRS will be done at Days 0 (baseline), 1, 2, 3, 4, 5, 8, 15, and 28. Baseline for each treatment period is the BPI-SF score taken before the injection on Day 0.

The BPI-SF is a 15-item self-rating scale assessing use of medications, as well as sensory, and reactive components of pain. The BPI-SF includes items that will address components of sensory pain, including severity, location, chronicity, and degree of relief due to therapy. The BPI-SF also has items that address reactive pain components, including depression, suffering, and perceived availability of relief. The BPI-SF also has items that address reactive pain components, including depression, suffering, and perceived availability of relief. Two BFI-SF scales will be derived from the BPI-SF responses: the pain severity score and pain interference score. The two BPI-SF parameters will be summarized by treatment period and day using descriptive statistics for observed, change from baseline, and percent change from baseline values.

7.11.4 Area under the effect curve over 28 days and maximum effect

The area under the effect curve over 28 days (AUEC28) and maximum effect (Emax) following the T1 (index) and T2 (repeat) injections will be calculated for cortisol levels, WBC counts, and fasting blood glucose levels.

AUEC28 will be compared for cortisol following index and repeat injections within the same subject to conclude whether or not repeat injection results in more pronounced cortisol suppression. This will be done using a two-sided paired T-test with the null mean being zero.

AUEC28 and Emax will be compared for cortisol, glucose, and WBC between index injection (treatment 1) and repeat injection (treatment 2) using a mixed model analysis of variance using PROC MIXED with a fixed effect for treatment (treatment 1 and 2) and a random effect for subject. Estimates and 90% confidence intervals (CIs) will be first constructed in the logarithmic scale. The response variable will be the change from pre-dose of each PD parameter. Treatment comparisons will be performed between treatments T1 and T2 with T2 being the reference. By taking anti-logarithms, estimates and CIs for the geometric means and ratios of geometric means will be calculated. All CIs will be 2-sided.

The statistical model will have the following form:

[redacted]

The following SAS code will be used to run the model;

[redacted]

[redacted]

The following SAS code will be used to calculate the geometric means, geometric ratio and its confidence interval:

[redacted]

A lack of effect of repeat injection on the PD will be concluded if the 90% CIs for the ratio of T2 (repeat injection; Test) to T1 (index; Reference) for both AUEC28 days and Emax are completely contained within the range of 80 to 125%.

7.12 Safety Analyses

The safety analyses will be presented by the treatment period for the Safety Analysis population.

7.12.1 Adverse Events

All AEs will be coded using the most current version of MedDRA. TEAEs and SAEs will be summarized descriptively for each treatment period.

A treatment emergent adverse event (TEAE) phase is defined as meeting either of the following 2 criteria:

- Any AE that has an onset on or after the index injection and within (after) 30 days of the last study treatment.
- Any pre-existing AE that has worsened in severity on or after the index injection and within (after) + 30 days of the last injection.

TEAEs for each treatment period, will be assessed as follows:

- A TEAE will be assigned to the treatment received immediately before onset.
- If the severity of a TEAE increases in a later period the TEAE at the increased severity will be assigned to the treatment received immediately before the increase in severity.

Onset date of adverse events on or post visit 3 but before visit 11 were considered as occurring during T1; otherwise onset date of adverse events on or post visit 11 were considered as occurring during T2

A treatment-related AE is defined as an AE as being possibly, probably or related to the study drug. If an AE has missing relationship it is assumed to be related to the study drug for analysis purposes.

Severity is classified as mild/moderate/severe/life-threatening/death (last two grades applied for SAE). If a subject reports AEs more than once within a SOC/PT, the AE with the worst-case severity will be used in the corresponding severity summaries. TEAE summary tables (except the overall summary table) will be presented by severity and overall.

The following tables will be presented by severity and overall for AEs:

- Overall incidence and the number of AEs, SAEs, TEAEs leading to withdrawal.
- Treatment-Emergent Adverse Event by System Organ Class and Preferred Term
- Related Treatment-Emergent Adverse Event by System Organ Class and Preferred Term
- Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
- Serious Treatment Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
- Treatment Discontinued Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
- Summary of Treatment-Emergent Adverse Events Leading to Death

All AEs will be listed.

7.12.2 Laboratory Data

Descriptive statistics of the observed values and change from baseline (continuous data) will be presented by treatment period and visit (Screening, T1 – Day 5, T1 – Day 28, T2 – Day 5, and T2 – Day 28 (Visit 19/EOS/ET)) for each hematology (Hemoglobin, hematocrit, red blood cell count, WBC count (with differential [lymphocytes, neutrophils, eosinophils, basophils, and monocytes]), and platelet count), serum chemistry (albumin, alkaline phosphatase, AST, ALT, direct bilirubin, total bilirubin, blood urea nitrogen, calcium, chloride, creatine kinase (Screening only), creatinine, gamma-glutamyl transferase, glucose, lactate dehydrogenase, potassium, sodium, and uric acid), and urinalysis (Dipstick analysis: color, turbidity, specific gravity, pH, glucose, protein, ketones, urobilinogen, bilirubin, blood nitrate, leukocyte esterase, and microscopic examination when

indicated by dipstick results) parameter. Each measurement (continuous data) will be classed as below, within, or above normal range, based on ranges supplied by the laboratory used. Shift tables in relation to the normal range from baseline to each follow-up visit will be presented.

The following lab parameters will be listed only. HbA1c, HIV, hepatitis B, and hepatitis C at Screening. Coagulation tests at Screening or Baseline: activated PTT, PT, INR, serum pregnancy test at Screening, urine pregnancy test at Baseline and at Visit 11 (T2 – Day 0), and MRI.

A listing of any clinically significant laboratory measurements recorded throughout the study will be presented.

7.12.3 Vital Signs and Body Weight

Descriptive statistics for observed values and changes from baseline in the following vital signs will be presented by treatment period and visit for T1 at Days 0 (baseline), 1, 2, 3, 4, 5, 8, 15, and 28, for T2 at Days 0 (baseline), 1, 2, 3, 4, 5, 8, 15, and 28.

- Systolic blood pressure (mmHg)
- Diastolic blood pressure (mmHg)
- Heart rate (bpm)
- Weight (kg)

Vital signs will be monitored within 15 min prior to the SP-102 injection, approximately every 5 min during the procedure (prior to syringe removal), and approximately every 15 min after for 60 min after the procedure. For Day 1 in both treatment periods, vital signs for three timepoints will be summarized:

Pre-injection: this is the value taken at 15 mins prior to the injection

During injection: this is the mean of the values taken during the injection procedure

Post-injection: this is the mean of the values recorded post injection

Vital sign values will be categorized into the following potential clinical concern categories if applicable and summarized.

Vital Sign	**Potential Clinical Concern Categories**
Systolic blood pressure	≥ 160 mmHg
Diastolic blood pressure	≥ 100 mmHg

Heart rate	< 60 or > 100 bpm

Vital signs data will also be listed.

7.12.4 Electrocardiogram Data

Since ECGs are collected in triplicates, the values will be averaged at each visit. ECGs will be assessed for T1 at Day 0 (baseline), Day 28, for T2 at Day 28. Descriptive statistics for observed values and changes from baseline in the following ECG variables will be tabulated at each follow-up:

- Heart rate (bpm)
- PR interval (ms)
- RR interval (ms)
- QRS duration (ms)
- QT interval (ms)
- QTc interval (ms)

Shift tables in relation to the overall interpretation (Normal, Abnormal NCS, and Abnormal CS) from baseline to each follow-up visit will be presented.

7.12.5 Physical Examination

A physical examination will be done at Screening, T1 – Day 0, T1 – Day 28, and T2 – Day 28 (Visit 19/EOS/ET). The results of the body systems within the physical examination data be summarized by treatment period and listed. A shift table will also be provided.

7.12.6 General Neurological and Targeted Neurological Examinations

General and targeted neurological examinations will be performed pre-dose and post dose on T1 – Day 1, pre-dose and post dose on T2 – Day 1, and on T2 – Day 28 (Visit 19/EOS/ET). The results will be summarized and listed.

8 INTERIM ANALYSIS

No interim analyses are planned.

9 DATA SAFETY MONITORING BOARD ANALYSIS

No data safety monitoring board (DSMB) analyses are planned.

10 CHANGES TO PLANNED PROTOCOL ANALYSIS

In the protocol, it is stated that: “No formal statistical hypothesis testing will be performed in this study, however descriptive statistics will be presented”. However, given that inferential analysis will be carried out on the PD data, this statement is disregarded.

11 LIST OF TABLES, FIGURES AND LISTINGS

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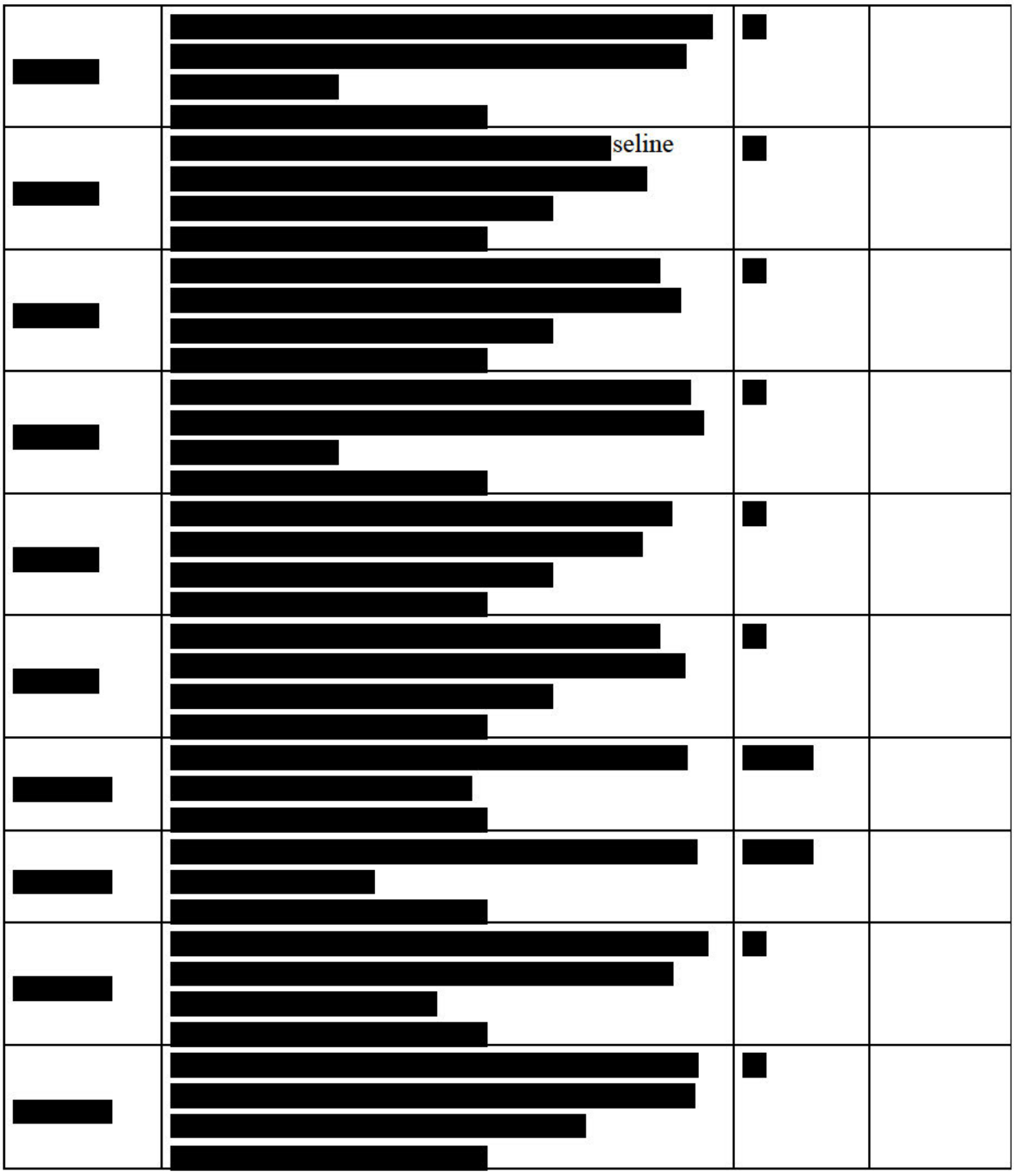
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12 REFERENCES

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