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STUDY HTX-100-403

A PHASE 4, OPEN-LABEL SAFETY STUDY OF REPEAT DOSES OF SUSTOL IN ADULT SUBJECTS RECEIVING CHEMOTHERAPY

01Nov2023

Statistical Analysis Plan

Version 1.0

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The undersigned approves the statistical analysis plan.

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List of Abbreviations

Abbreviation	Term
ADL	Activities of daily living
AE	Adverse event
CAISR	Clinical Assessment of Injection Site Reactions
ClinRO	Clinician-reported outcomes
CRO	Contract research organization
CTCAE	Common Terminology Criteria for Adverse Events
DISRA	Daily Injection Site Reaction Assessment
DM	Data management
DSMB	Data Safety Monitoring Board
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic case report form
ePRO	Electronic patient-reported outcome
ISR	Injection-site reaction
MedDRA	Medical Dictionary for Regulatory Activities
SAE	Serious adverse event
SAP	Statistical analysis plan
TEAE	Treatment-emergent adverse event
USPI	United States prescribing information
WHODrug	World Health Organization Drug Dictionary

1. ADMINISTRATIVE STRUCTURE

1.1. Sponsor and Oversight

This study is being conducted under the sponsorship of Heron Therapeutics, Inc. (Heron). The data management (DM) is being performed by Heron and the statistical analyses are being performed under contract with EMB Statistical Solutions (EMB), with oversight from Heron. EMB is a contract research organization (CRO).

1.2. Data Quality Assurance

The Biostatistics and Programming group at the CRO will collaborate with the Sponsor to ensure that the data collected and analyzed for this study are of the highest quality possible and meet the data standards set for the study. This will be accomplished in part through programmed edit checks, which will be reviewed by the data managers, statisticians, programmers, and other team members on an ongoing basis to evaluate whether any checks need to be added or any existing checks need to be modified. In addition, periodic reviews of listings of accumulating data, assessment of data query trends, and resulting retraining of study site personnel, as applicable, will be performed to further ensure data quality.

2. INTRODUCTION

This statistical analysis plan (SAP) presents a detailed plan of the statistical methods to be used during the reporting and analysis of data collected in this study. Revisions can be made to this SAP while the study is ongoing; however, it must be finalized prior to database lock. Any deviations from the analysis plan provided in the SAP will be fully documented in the final Clinical Study Report.

This SAP should be read in conjunction with the study protocol and the electronic case report forms (eCRFs).

3. OBJECTIVES

Primary Objective:

To characterize the potential impact of subject-reported injection-site reactions (ISRs) on activities of daily living (ADL) in adult subjects with cancer administered SUSTOL.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is a Phase 4, open-label safety study of SUSTOL in adult subjects with cancer receiving moderately emetogenic chemotherapy or anthracycline and cyclophosphamide combination chemotherapy regimens. Subjects will be screened for study eligibility up to 21 days prior to receiving their first dose of SUSTOL. Approximately 300 subjects will be enrolled. Subjects who meet eligibility requirements will be enrolled and receive SUSTOL (administered 10 mg SC) per the United States prescribing information (USPI) on Cycle 1 Day 1, and on Day 1 of up to 3 subsequent cycles. SUSTOL will be administered in combination with dexamethasone at least 30 minutes before the initiation of chemotherapy.

4.2. Assessments

Safety assessments will be performed. The start of study drug administration will be considered Time 0 for all assessments.

Safety Assessments

- ePRO DISRA (Electronic patient-reported outcome, Daily Injection Site Reaction Assessment).
- ClinRO CAISR (Clinician-reported outcomes, Clinical Assessment of Injection Site Reactions).
- TEAEs (evaluated by the clinician using the Common Terminology Criteria for Adverse Events [CTCAE] toxicity grade categories) that:
  - Led to discontinuation of SUSTOL treatment.
  - Led to withdrawal from the study.
- SAEs (evaluated by the clinician using the CTCAE categories).
- Physical examinations.
- Vital signs, including blood pressure, resting heart rate, respiratory rate, and body temperature.
- ECOG performance status.
- Clinical laboratory tests.

4.3. Endpoints

4.3.1. Primary Endpoint

- Proportion of subjects with a subject-reported ISR composite dichotomous (0 or 1) score of 1 defined as follows:
  - ISR of pain, itching, or swelling with a severity ≥7 **AND** ADL impact of ≥7 in any ADL domain (physical, social, work/household).
    OR

- ISR of bleeding with ADL impact of ≥7 in any ADL domain (physical, social, work/household), **AND** 1 of the following:
  - severity ≥7 and 4 to 6 bandage changes per day **OR**
  - ≥7 bandage changes per day **OR**
  - urgent care/ER visit

4.3.2. Secondary Endpoints

- Proportions of subjects with ISR-related SAEs and with ISR-related TEAEs that led to discontinuation of SUSTOL treatment or withdrawal from the study.
- Proportions of subjects with SAEs and TEAEs that led to discontinuation of SUSTOL treatment or withdrawal from the study, of any cause.
- Proportions of subjects with ISRs that led to delay of chemotherapy treatment.
- Proportion of subjects with a subject-reported ISR for each ISR category by maximum severity, by cycle and overall.
- Proportion of subjects with a subject-reported ISR by highest level of impact on each ADL domain, by cycle and overall.
- Proportion of subjects with an ISR requiring healthcare utilization.
- Proportion of subjects with an ISR requiring intervention (surgical, other).
- Mean duration (days) of each subject-reported ISR, by cycle and overall.
- Mean maximum size of each clinician-reported ISR (nodules, erythema, ecchymosis and hematomas) by cycle and overall.
- Proportion of subjects with a subject-reported ISR pain severity ≥7 AND presence of each or any of ClinRO CAISR signs (nodule, hematoma, erythema, ecchymosis, infection, ulceration, or necrosis).

5. GENERAL STATISTICAL CONSIDERATIONS

Continuous data will be presented using descriptive statistics: number of subjects (n), mean, standard deviation (SD), median, minimum and maximum. Categorical data will be summarized by the number and percent of subjects. Data will be displayed in all listings sorted by subject number, cycle, and visit/study day. When count data are presented, the percent will be suppressed when the count is zero in order to draw attention to the non-zero counts. A row denoted “Missing” will be included in count tabulations where necessary to account for dropouts and missing values. The denominator for all percentages will be the number of subjects in the population of interest, unless otherwise stated. Non-zero percentages will be rounded to one decimal place, except 100% will be displayed without any decimal places. Additional rounding rules are as follows:

- If the original value has 0 decimal places: mean and median will have 1 decimal place and SD and SE will have 2 decimal places

- If the original value has 1 decimal place: mean and median will have 2 decimal places and SD and SE will have 3 decimal places
- If the original value has 2 or more decimal places: mean, median, SD, and SE will all have 3 decimal places

Minimum and maximum will always have the same decimal places as the original measure, up to a maximum of 3 decimal places. The above rounding rules will not be applied to original measures displayed in listings.

Values that are collected with "<" or ">" signs will be analyzed as the numerical value without the sign in tables and figures. In listings, these data will be reported as collected with the sign.

All safety data will be entered in the electronic data capture system. Datasets will be created using the Study Data Tabulation Model (SDTM) v. 1.4 or higher, conforming to the SDTM Implementation Guide (SDTMIG) v. 3.2 or higher. Datasets, tables, listings, and figures will be programmed using SAS® v. 9.4 or higher. All safety data will be listed via the SDTM datasets and selected safety data will be listed via programmed listings.

All demographic and safety analyses will be performed using descriptive statistics.

5.1. Sample Size

Approximately 300 subjects will be enrolled, with approximately 100 subjects anticipated to experience an ISR. The sample size is based on anticipation of a 33% rate of ISRs that may potentially impact subject ADL. This rate was estimated from the results of a prospective, randomized, active-controlled, double-blind Phase 3 study that included a patient diary to record ISRs, in which the highest ISR rate associated with a grade reported to interfere with activities was approximately 33% for pain.

5.2. Randomization, Stratification, and Blinding

This is an open-label study. All subjects who meet eligibility requirements will receive SUSTOL in this single−arm study.

5.3. Analysis Populations

5.3.1. Safety Population

The Safety Population will consist of all subjects who receive at least 1 dose of study drug. This population will be used for all demographic, baseline characteristics, and safety summaries.

5.4. Other Important Considerations

5.4.1. Study Day Calculation for Reporting Purposes

The following convention will be used to calculate study day for reporting purposes:

- The study day of first study drug administration is Study Day 1
- For measurements that are *on or after* the date of first study drug administration:
  - Study Day = date of measurement – date of first study drug administration + 1
- For measurements that are *prior* to the date of first study drug administration:
  - Study Day = date of measurement – date of first study drug administration

5.4.2. Handling of Missing and Partial Data

No imputations for missing values should be used for DISRA and CAISR item responses; analysis will be based on observed data. DISRA completion date is based on the subject's data entry date. If this data is not entered by the subject, then DISRA completion date will be derived based on the ePRO DISRA form name where a visit day relative to dosing is indicated. Ad-hoc DISRA visit will be categorized under a cycle based on whether the ad-hoc DISRA was entered after the study drug injection date during that cycle and before the study drug dosing of next cycle.

All safety results will be summarized using observed cases with no imputation.

For partial dates involving AE start dates and concomitant medication start dates, the algorithms for imputation will vary depending upon the parameter; the details can be found in Appendix 1. No other partial dates will be imputed.

6. SUBJECT DISPOSITION

A summary of disposition of subjects will include the number and percentage of subjects for the following categories: subjects enrolled (signed and dated the informed consent form), subjects who failed screening with reasons for screen failure, subjects in the Safety Population, subjects completing the study, and subjects not completing the study by reason for withdrawal. Only 1 reason for study withdrawal will be recorded for each subject.

7. DEMOGRAPHICS, CHARACTERISTICS, AND MEDICAL HISTORY

7.1. Demographics and Baseline Characteristics

Demographics and baseline characteristics will be presented in tables using descriptive statistics. Demographics consist of age, age category, sex, race, and ethnicity. Baseline

characteristics consist of weight, height, and body mass index (BMI). A subject's age in years is calculated using the integer part of the difference in number of days between the date that informed consent is signed and dated and date of birth divided by 365.25, or is recorded directly on the eCRF. The number and percentage of subjects in the following age categories will be presented: 18-44, 45-54, 55-64, 65-74, 75-84, and ≥ 85 years.

Demographics and baseline characteristics will be presented for the Safety Population.

7.2. Medical History

Medical history will be coded using the Medical Dictionary for Regulatory Activities (MedDRA®) version 24.1. Medical history will be summarized for the Safety Population and will display the number and percentage of subjects with a past and/or concomitant disease or surgeries by System Organ Class (SOC) and Preferred Term (PT).

7.3. Protocol Deviations

Deviations from the protocol will be recorded. Prior to database lock, protocol deviations will be categorized as described in the Protocol Deviation Management Plan.

Classification of deviations as important protocol violations will be decided on a case-by-case basis using the criteria specified in the Protocol Deviation Management Plan. All protocol deviations and important protocol deviations will be presented in a summary table by protocol deviation category for the Safety Population.

8. TREATMENTS AND MEDICATIONS

8.1. Prior and Concomitant Medications

Prior medications are defined as medications with a stop date occurring before Study Day 1. Concomitant medications are defined as medications that are ongoing on Study Day 1 or with a start date occurring on or after Study Day 1. Medications with start and stop dates which bracket Study Day 1, or for which missing start and/or stop dates make it impossible to determine the prior or concomitant status, will be summarized as concomitant medications.

All medications will be coded with the World Health Organization Drug Dictionary Global B3 Format (WHODrug Global B3), September 2021.

Prior and concomitant medications will be summarized separately by drug class and generic drug name. At each level of summarization, a subject is counted once if that subject reports 1 or more medications at that level. Drug class will correspond to the Anatomical Therapeutic Classification (ATC) Level 2 term.

All prior and concomitant medications will be summarized for the Safety Population.

8.2. Study Treatment

A single dose of study drug SUSTOL 10 mg will be administered subcutaneously on the first day of each chemotherapy cycle at least 30 minutes before the start of emetogenic chemotherapy. Number of SUSTOL injections will be summarized. Number of chemotherapy cycles initiated will also be summarized. SUSTOL injection date/time, injection site location, and chemotherapy start date/time will be presented by subject number, and chemotherapy cycle in a data listing.

9. SAFETY ANALYSIS

All analyses of safety data will be conducted using the Safety Population. Statistical hypothesis testing will not be performed on any safety results. No imputation of missing safety data will be performed except in the case of partial AE, concomitant medication onset dates (Appendix 1). and missing DISRA completion date from the EDC (Section 5.4.2).

9.1. ePRO DISRA

The occurrence, severity, and potential impact of subject-reported ISRs on ADL will be evaluated using an electronic patient-reported outcome (ePRO) Daily Injection Site Reaction Assessment (DISRA).

The ePRO DISRA will collect the presence or absence of ISRs, the severity of each ISR (0-10 scale, with 0 indicating no pain/bleeding/itching/or swelling, and 10 indicating worst possible pain/bleeding/itching/or swelling), and the perceived impact of the ISR on the subject's ADL (0-10 scale, with 0 indicating no interference and 10 indicating extreme interference) using the following ISR categories and ADL domains:

ISRs:

- Pain.
- Bleeding.
- Itching.
- Swelling.

ADL domains:

- Physical.
- Social.
- Work/household.

9.2. ClinRO CAISR

At each site visit, the site staff will use the clinician-reported outcomes (ClinRO) Clinical Assessment of Injection Site Reactions (CAISR) to assess the following:

The presence or absence of any ISR-related:

- Nodule.
- Erythema.
- Ecchymosis.
- Hematoma.
- Infection.
- Ulceration.
- Necrosis.

The size of:

- Nodules.
- Erythema.
- Ecchymosis.
- Hematomas.

Additionally as part of the ClinRO CAISR, ISR-associated healthcare resource utilization (eg, emergency room [ER], urgent care, unscheduled clinic visit), intervention (surgical or other) and ISRs that led to delay of chemotherapy treatment or discontinuation of SUSTOL or withdrawal from study will also be recorded.

9.3. Adverse Events

An AE is defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. An AE may be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a study drug, whether or not considered causally associated with the use of the study drug.

For an event to be a TEAE, it must meet one of the following conditions:

- Begins on Study Day 1, during or after administration of study drug
- Begins after Study Day 1

- Begins before Study Day 1 and worsens in severity during or after the Study Day 1 administration of study drug

AEs with unknown onset dates or unknown end dates will be counted as TEAEs unless the event resolves before Study Day 1.

AEs will be coded using MedDRA version 24.1.

9.4. Safety Analyses

9.4.1. Primary Analysis

For the primary endpoint of a composite score based on subject-reported ISRs, a subject will be classified as either having a score of 1 or 0 based on ePRO DISRA from up to 4 sequential cycles of chemotherapy. The overall composite score for a patient is,

- 1, if the score from any of the visits is 1;
- 0, otherwise

At any visit, subjects need to meet both of the severity and impact criteria specified in Section 4.3.1 at the same visit from the same ISR (pain/itching/swelling) in order for them to be classified as having a score of 1 for that visit. Similarly for ISR of bleeding, the criteria on severity and either of the impact or bandage changes or urgent care/ER visit need to be met during the same visit for a subject to be classified as having a score of 1 for that visit.

The composite primary endpoint score will be summarized and presented in a subject listing. A 95% confidence interval will be provided for the proportion of subjects with a score of 1.

9.4.2. Secondary Analyses

9.4.2.1. Incidence of Treatment-Emergent Adverse Events (TEAEs)

The incidence of TEAEs table will include only 1 occurrence of a PT per subject. For a given PT, if a subject reports that PT multiple times, that subject will only be counted once since unique subject counts will be presented. Similar to the analysis of PTs, for a given SOC if a subject reports multiple TEAEs within the same SOC, that subject will only be counted once at the SOC level since unique subject counts will be presented. SOCs will be sorted by the internationally agreed order and PTs will be sorted within SOC in descending order of incidence.

An overall summary of TEAEs will be presented, and will include the following:

- Number of subjects with at least 1 TEAE that led to discontinuation of SUSTOL treatment or withdrawal from the study
- Number of subjects with at least 1 SAE

- Number of subjects with at least 1 ISR-related TEAE that led to discontinuation of SUSTOL treatment or withdrawal from the study
- Number of subjects with at least 1 ISR-related SAE

The incidence of TEAEs will be presented by SOC and PT. The incidence of TEAEs will be also presented by PT.

9.4.2.1.1. TEAEs Leading to Discontinuation of SUSTOL Treatment or Withdrawal from the Study

All TEAEs reported with "Study Drug Discontinued" or "Withdrawal from Study" checked on the eCRF will be presented in a table by SOC and PT and in a table by PT. The AE data will be presented in a listing.

9.4.2.1.2. SAEs

SAEs will be presented in a table by SOC and PT and in a table by PT. Data listing for the SAEs will also be presented.

9.4.2.1.3. ISR-related TEAEs Leading to Discontinuation of SUSTOL Treatment or Withdrawal from the Study

TEAEs reported as "ISR-related" with "Study Drug Discontinued" or "Withdrawal from Study" checked on the eCRF will be presented in a table by SOC and PT and in a table by PT. The ISR-related TEAEs will be presented in a data listing.

9.4.2.1.4. ISR-related SAEs

SAEs reported as "ISR-related" will be presented in a table by SOC and PT and in a table by PT. Data listing will be presented for the ISR-related SAEs.

9.4.2.1.5. Death

Any subject deaths during this study will be collected and presented in a listing. The information that is presented will include date of death, days on study, days since last SUSTOL injection, cause of death, and relationship of death to study drug.

9.4.2.2. ISR Leading to Delay of Chemotherapy Treatment (CAISR)

Subjects with chemotherapy cycle delayed due to SUSTOL ISR as reported in CAISR will be summarized by cycle and overall. The endpoint will be presented as part of the CAISR data listing.

9.4.2.3. Subject-reported ISR Categories (DISRA)

Subjects report ISR in the four categories in DISRA: Pain, Bleeding, Itching, and Swelling. Subjects with ISR will be summarized for each ISR category by maximum of the daily assessed worst severity, by cycle and overall. The ISR report will be present in the DISRA data listing.

9.4.2.4. Subject-reported ISR Impact on ADL (DISRA)

ISR impacts are reported in the three domains of activities of daily living (ADL) in DISRA: Physical, Social, and Work/Household. Subjects with ISR will be summarized for each ADL domain by highest level of impact on each ADL domain, by cycle and overall. The ISR impact on ADL will be presented in the DISRA data listing.

9.4.2.5. ISR Requiring Healthcare Utilization (CAISR)

ISRs requiring healthcare utilization, including Emergency Room, Urgent Care, Unscheduled Clinic Visit, and Extra Healthcare Utilization during a Required Study Visit, are reported in CAISR. Subjects with ISRs requiring healthcare utilization and the types of healthcare utilization (emergency room, urgent care, unscheduled clinic visit and extra healthcare utilization during a required study visit) will be summarized by cycle and overall. The assessment will be presented as part of the CAISR data listing.

9.4.2.6. ISR Requiring Intervention (CAISR)

ISRs requiring surgical or other intervention are reported in CAISR. Subjects with ISR requiring intervention will be summarized by cycle and overall. The assessment will be presented as part of the CAISR data listing.

9.4.2.7. Mean duration of Each Subject-reported ISR Category (DISRA)

Duration of an ISR is defined as the total number of days a subject reported an ISR in a cycle. Duration in days of each subject-reported ISR category by cycle and mean duration over all cycles will be summarized. The mean duration calculated for a subject's each ISR category by cycle and overall will be presented in a data listing.

9.4.2.8. Size of Each Clinician-reported ISR (CAISR)

The size of ISR signs including Nodule, Hematoma, Erythema, and Ecchymosis is reported by clinician for each cycle. The maximum size for each of the four ISR signs from all cycles and the size by cycle will be summarized. The assessment will be presented as part of the CAISR data listing.

9.4.2.9. Subjects With ISR Pain Severity ≥7 (DISRA) AND Clinician-Reported ISRs (CAISR)

Subjects With ISR pain severity ≥7 (DISRA) and clinician-reported ISRs (CAISR) will be summarized and listed.

9.4.3. Other Safety Analyses

9.4.3.1. Clinical Laboratory Results

Laboratory assessments will be performed by a local laboratory (hematology and serum chemistry) at Screening, Day 1 of each cycle, any rescreen and unscheduled visit.

Creatinine clearance data will be summarized in a table and also presented in a data listing.

Laboratory results accounting for TEAE(s) meeting the criteria listed in Section 9.4.2.1 will be presented in a data listing.

Listings of laboratory values will include flags for values outside the local laboratory normal ranges that indicate how far out of the normal range a value is. For example, a value that is ≥ 3 times the upper limit of normal (ULN) but below 4 times the upper limit of normal will have a "3H" flag. Flag multipliers will show values that are 1, 2, 3, 4, 5, and 10 times relative to the ULN if high. Values that are below the lower limit of normal (LLN) will be flagged simply with "L".

9.4.3.2. Vital Signs

Vital signs including systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate/pulse (HR), body temperature, and respiration rate will be collected at Screening, Day 1 of each cycle, any rescreen and unscheduled visit.

Vital signs assessments will be summarized by scheduled visits. All vital signs data will be presented in a data listing.

9.4.3.3. ECOG Performance Status

ECOG performance status assessment will be performed at Screening, Baseline, Early Termination, and Final Follow-Up Visit. The results will be summarized by scheduled visits. All ECOG performance assessments will be presented in a data listing.

9.4.3.4. Physical Examination

Physical examination will be performed at Screening, any rescreen and unscheduled visit. Physical examination data will be listed only.

10. INTERIM ANALYSIS

10.1. Interim Analysis

No formal interim analyses are planned.

10.2. Data Safety Monitoring Board

An independent Data Safety Monitoring Board (DSMB) will not be involved with the conduct of this study. Investigators are responsible for the detection, assessment, and documentation of AEs, including SAEs, unanticipated problems, and pregnancies.

Investigators must review the current SUSTOL prescribing information as well as the current prescribing information for other protocol-specified medications to be aware of the safety-related events that may be anticipated with their use.

11. REFERENCES

SUSTOL USPI. SUSTOL® (granisetron) extended-release injection, for subcutaneous use. San Diego, CA: Heron Therapeutics, Inc; 2017.

APPENDIX 1. IMPUTATION OF PARTIAL AND MISSING DATES

Incomplete Dates of Adverse Event start

All AE onset dates must be entered on the eCRF as complete dates. In the rare case that all or part of an AE onset date is missing but an AE resolution date is present and after study drug administration then the AE onset date will be imputed as follows:

Year of onset	Month of onset	Day of onset	Onset date to be imputed as
Missing	Missing	Missing	Date of SDA
year = year of SDA	Missing	Nonmissing	Date of SDA
year = year of SDA	Missing	Missing	Set month and day to those of SDA
year < year of SDA	Missing	Nonmissing	set month to December
year < year of SDA	Missing	Missing	set month and day to December 31
year > year of SDA	Missing	Nonmissing	set month to January
year > year of SDA	Missing	Missing	set month and day to January 1
year = year of SDA	Month = month of SDA	Missing	Set day as day of SDA
year = year of SDA	Month < month of SDA	Missing	Set day as last day of onset month
year = year of SDA	Month > month of SDA	Missing	Set day as first day of onset month
year < year of SDA	Nonmissing	Missing	Set day as last day of onset month
year > year of SDA	Nonmissing	Missing	Set day as first day of onset month

SDA = study drug administration.

If AE resolution date is present and prior to study drug administration, no need to impute incomplete AE start date, as the AE is not treatment emergent and the event should be in the medical history.

Concomitant Medications

- If year and month are present and day is missing then set day to first day of month for start date, and set day to last day of month for end date
- If year and day are present and month is missing then set month to January for start date, and set month to December for end date
- If year is present and month and day are missing then set month and day to January 1 for start date, and set month and day to December 31 for end date
- Completely missing dates will not be imputed

If start date is completely missing and end date is not prior to study drug administration, then the medication will be classified as concomitant; if the end date is missing, then the medication will be classified as ongoing. Medications for which the start and end dates are completely missing will be classified as concomitant.

APPENDIX 2. DOCUMENT REVISION HISTORY

Version	Date	Notes/Revisions
1.0	01Nov2023	Initial version, based on protocol version 1 (23AUG2021)

Signature Page for VV-CLIN-006854 v1.0

Approval Task	[redacted] 15-Jan-2026 19:45:16 GMT+0000

Signature Page for VV-CLIN-006854 v1.0