A Phase 2, Multicenter, Open-label, Proof of-Concept Study with Safety Run-in to Evaluate the Safety, Pharmacokinetics, and Efficacy of VP-315 in Adult Subjects with Basal Cell Carcinoma

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Statistical Analysis Plan

Protocol Title	A Phase 2, Multicenter, Open-label, Proof-of-concept Study with Safety Run-in to Evaluate the Safety, Pharmacokinetics, and Efficacy of VP-315 in Adult Subjects with Basal Cell Carcinoma
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SAP Author	Carrie Kaempfer Manager, Biostatistics Veristat LLC

This study will be conducted in compliance with the protocol, Good Clinical Practice, and all other applicable regulatory requirements, including the archiving of essential documents.

SAP Document History

Version	Author	Date	Change
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Signatures / Approvals

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List of Abbreviations

AE	Adverse Event
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Chemical
ATCC	ATC Classification
AUC	Area under the plasma concentration-time curve
BCC	Basal Cell Carcinoma
BMI	Body Mass Index
BP	Blood Pressure
BUN	Blood Urea Nitrogen
CRA	Cutaneous Reaction Assessment
CS	Clinically Significant
CSR	Clinical Study Report
CV	Coefficient of Variation
DLT	Dose-limiting Toxicity
DMP	Data Management Plan
Dy	Day y, where y = 1, 2, 3
ECG	Electrocardiogram
EDC	Electronic Data Capture
EOS	End of Study
EOT	End of Treatment
FACE-Q	Patient-reported outcome measure for facial procedures
FA	Full Analysis
ICH	International Conference on Harmonization
LDH	Lactic Dehydrogenase
LLQ	Lower Limit of Quantitation
MCHC	Mean Corpuscular Hemoglobin Concentration
MCV	Mean Corpuscular Volume
MedDRA	Medical Dictionary for Regulatory Activities
MTD	Maximum Tolerated Dose

NCS	Not Clinically Significant
NTL	Non-target Lesion
PGA	Physician Global Assessment
PK	Pharmacokinetic
PN	Preferred Name
PP	Per-protocol
PT	Preferred Term
RBC	Red Blood Cell Count
RT	Reported Term
SCAR	Scar Cosmesis Assessment and Rating Questionnaire
SCAR-Q	Patient-reported outcome measure for scars (Note: not SCAR)
SAE	Serious Adverse Event
SAF	Safety
SAP	Statistical Analysis Plan
SD	Standard Deviation
SGOT	Serum Glutamic Oxaloacetic Transaminase
SGPT	Serum Glutamic Pyruvic Transaminase
SOC	System Organ Class
SRC	Safety Review Committee
TEAE	Treatment-emergent Adverse Event
TL	Target Lesion
TRAE	Treatment-related Adverse Event (same as related TEAE)
TRAE SI	TRAE of Special Interest
ULQ	Upper Limit of Quantitation
WBC	White Blood Cell Count
WxDy	Week x Day y, where x = 1, 2 and y = 1, 2, 3
WHO	World Health Organization
Wx	Week x, where x = 1, 2

1. Introduction

This Statistical Analysis Plan (SAP) describes the planned analysis and reporting for Verrica Pharmaceuticals Inc. protocol number VP-315-201 entitled "A Phase 2, Multicenter, Open-label, Proof-of-concept Study with Safety Run-in to Evaluate the Safety, Pharmacokinetics, and Efficacy of VP-315 in Adult Subjects with Basal Cell Carcinoma."

This is an open-label, multicenter, proof-of-concept study with a safety run-in designed to assess the safety, tolerability, maximum tolerated dose (MTD), and objective antitumor efficacy of VP-315 when administered intratumorally to adults with biopsy-proven basal cell carcinoma (BCC).

Conveyed in this SAP are the planned analyses of the primary, secondary, and exploratory endpoints. This SAP and any modifications or changes must be finalized before the database is locked.

2. Objectives and Endpoints

The following objectives and endpoints will be considered.

Part 1	
Primary Objectives	**Endpoints**
• To assess the safety, tolerability, and maximum tolerated dose (MTD) of ascending dose strengths of VP-315	• Discontinuations due to adverse events (AEs); occurrence of dose-limiting toxicities (DLTs) • Cutaneous Reaction Assessment (CRA)
Exploratory Objectives	**Endpoints**
• To evaluate the objective antitumor efficacy of VP-315	• Histological clearance of treated lesion(s) at excision • Clinical clearance of treated lesion(s) as determined by visual assessment (no tumor seen upon visible inspection) at excision • Estimate of remaining tumor volume (necrotic cells:tumor cells) at excision • Estimate of reduction in tumor volume (necrotic cells:tumor cells) at excision* • Abscopal effect as determined by

	clinical and histological clearance of nontreated lesions at excision ● Physician Global Assessment (PGA)
Part 2 (Cohorts 1 and 2)	
Primary Objectives	**Endpoints**
● To determine the optimal regimen for dosing 8 mg of VP-315 based on safety and tolerability	● Treatment-related AEs; treatment-related serious adverse events (SAEs); discontinuations due to AEs; occurrence of TRAEs of special interest ● CRA
Secondary Objectives	**Endpoints**
● To evaluate the antitumor efficacy of VP- 315	● Clinical clearance of treated lesion at excision as determined by visual assessment (no residual tumor seen on visual inspection) ● Histological clearance of treated lesion(s) at excision ● Abscopal effect as determined by clinical and histological clearance of nontreated lesions at excision if nontreated lesions exist ● Estimate of remaining tumor volume (necrotic cells:tumor cells) at excision ● Estimate of reduction in tumor volume (necrotic cells:tumor cells) at excision* ● PGA
Exploratory Objectives	**Endpoints**
● To assess the immune response to VP-315 treatment in a subset of subjects by assessing the immune repertoire in blood and in tissue	● Multiplex immunohistochemical staining for T-cell subsets and immune activation markers in tumor tissue samples ● Analysis of T-cell clonality in blood and tumor tissue samples
● To assess subject satisfaction with the treatment	● SCAR-Q, FACE-Q
Part 2 (Cohorts 4 and 5)	
Primary Objectives	**Endpoints**
● To gain additional information on the	● Treatment-related AEs; treatment-

safety, tolerability, and dosing regimen of VP-315 to support a pivotal study protocol design	related serious adverse events (SAEs); discontinuations due to AEs; occurrence of TRAEs of special interest ● CRA
Secondary Objectives	**Endpoints**
● To confirm the antitumor efficacy of VP- 315 using the optimal dosing regimen determined in Part 2	● Clinical clearance of treated lesion at excision as determined by visual assessment (no residual tumor seen on visual inspection) ● Histological clearance of treated lesion(s) at excision ● Abscopal effect as determined by clinical and histological clearance of nontreated lesions at excision if nontreated lesions exist ● Estimate of remaining tumor volume (necrotic cells:tumor cells) at excision ● Estimate of reduction in tumor volume (necrotic cells:tumor cells) at excision* ● PGA
● To characterize the pharmacokinetics (PK) of an 8 mg dose of VP-315 administered with the optimal dosing regimen determined in Part 2.	● Plasma VP-315 concentrations
Exploratory Objectives	**Endpoints**
● To assess subject and physician satisfaction with the treatment	● SCAR-Q, FACE-Q ● Scar Cosmesis Assessment and Rating (SCAR) Scale
● To assess the immune response to VP-315 treatment in a subset of subjects by assessing the immune repertoire in blood and in tissue	● Multiplex immunohistochemical staining for T-cell subset and immune activation markers in tumor tissue samples ● Analysis of T-cell clonality in blood and tumor tissue samples

*Additional endpoint not included in protocol. Further details are included in section 14.

3. Study Design

This is a two-part study with sequential enrollment. All enrolled subjects will receive VP-315 intratumoral injections on an outpatient basis into up to two target lesions (TLs) and up to three non-target lesions (NTLs) will not be injected. Dosing will commence in a single TL. This study was expected to enroll approximately 80 subjects with a histologic diagnosis of BCC in at least one eligible TL (confirmed by punch or shave biopsy). Up to 15 study sites in the US will participate. The Schedule of Assessments can be found in Section 8.3 of the protocol.

3.1. Part 1 (N = 10)

Subjects are to receive VP- 315 via once-daily dosing, with a starting total daily dose of 2 mg for the first cohort, escalating in 1 mg increments for subsequent cohorts after the current cohort has completed Week 1 dosing (the DLT observation period) and no DLT is observed. The planned dosing regimen is a split dose of VP-315 for all treatments. The ≤500µL (≤8 mg) dose is to be divided into 2 injections given at least 15 minutes and no more than 30 minutes apart, with 30% (≤150 µL) administered in the first injection and the remaining 70% (≤350 µL) with the second injection.

Subjects are to be treated until the lesion is necrosed or a DLT occurs, for a maximum of 2 weeks (W1D1, W1D2, W1D3 and W2D1, W2D2, W2D3 – up to 6 total doses increasing from the starting dose in 1 mg increments) and a maximum total daily dose of 8 mg. If the treated lesion necrosed and the subject has additional lesions, treatment of the next lesion may begin on D1 of the next week. A maximum of 2 TLs may be treated, and only 1 lesion may be treated at a time. DLT or visual confirmation of necrosis of all TLs will result in termination of VP-315 dosing.

3.2. Part 2 (N = 82)

Subjects receive VP-315 via once-daily dosing, which is to be a total daily dose of 8 mg in up to 5 cohorts (i.e., there were no DLTs that occurred during Part 1, and the maximum dose of 8 mg was achieved).

3.3. Cohort 1 (N = 6)

Subjects receive VP-315 via once-daily dosing of 8 mg with a loading dose of half the target dose of 8 mg (i.e., 4 mg) only on W1D1; all remaining doses are to be the full target dose without a loading dose. Subjects are to be treated until the lesion is necrosed, for a maximum of 2 weeks (W1D1, W1D2, W1D3 and W2D1, W2D2, W2D3 – up to 6 total doses). If the treated lesion necrosed and the subject has additional lesions,

treatment of the next lesion may begin on D1 of the next week. A maximum of 2 TLs may be treated, and only 1 lesion may be treated at a time.

3.4. Cohort 2 (N = 3)

Subjects receive VP-315 via once-daily dosing of 8 mg on all treatment days (i.e., no loading dose on W1D1). Subjects are to be treated until the lesion is necrosed, for a maximum of 2 weeks (W1D1, W1D2, W1D3 and W2D1, W2D2, W2D3 – up to 6 total doses). If the treated lesion necrosed and the subject has additional lesions, treatment of the next lesion may begin on D1 of the next week. A maximum of 2 TLs may be treated, and only 1 lesion may be treated at a time.

3.5. Cohort 3 (N = 0)

This cohort has been removed at the recommendation of the Safety Review Committee (SRC).

3.6. Cohort 4 (N = 36 [10 initial / 26 expansion] at two times weekly dosing)

Subjects receive VP-315 via once-daily dosing of 8 mg, administered on 2 consecutive days in one week (W1D1, W1D2). The planned dosing regimen is a split dose of VP-315 for all treatments. The 500µL (8 mg) dose is to be divided into 2 injections given at least 15 minutes and no more than 30 minutes apart, with 30% (150 µL) administered in the first injection and the remaining 70% (350 µL) with the second injection. Treatment for a second TL may begin on D1 of the next week (W2D1, W2D2). Each individual TL is treated for the assigned 2 days only (regardless of necrosis status). Up to 2 TLs may be treated – up to 4 total doses. Subjects with only 1 TL who complete week one of treatment without complete necrosis receive no additional treatment.

3.7. Cohort 5 (N = 37 [10 initial / 27 expansion] at three times weekly dosing)

Subjects receive VP-315 via once-daily dosing of 8 mg, administered on 3 consecutive days in one week (W1D1, W1D2, W1D3). The planned dosing regimen is a split dose of VP-315 for all treatments. The 500µL (8 mg) dose is to be divided into 2 injections given at least 15 minutes and no more than 30 minutes apart, with 30% (150 µL) administered in the first injection and the remaining 70% (350 µL) with the second injection. Treatment for a second TL may begin on D1 of the next week (W2D1, W2D2, W2D3). Each individual TL is treated for the assigned 3 days only (regardless of necrosis status). Up to 2 TLs may be treated – up to 6 total doses. Subjects with only 1 TL who complete week one of treatment without complete necrosis receive no additional treatment.

4. Dose-limiting Toxicity and Treatment-related Adverse Event of Special Interest

For Part 1 of the study, a dose-limiting toxicity (DLT) is defined as any of the following treatment-related adverse events (TRAEs) that occurs during the DLT period.

For Part 2 of the study, a treatment-related adverse event of special interest (TRAE SI) is defined as any TRAE that occurs during the treatment visit and meets the criteria below.

4.1. Treatment-related Adverse Events

TRAEs are treatment-emergent adverse events that are related to study treatment. Adverse events (AEs) considered DLTs (Part 1) or TRAEs SI (Part 2) are defined as follows. AEs considered DLTs or TRAEs SI are captured in EDC.

- Hypotension meeting any of the following definitions:
  - > 20 mmHg decrease in systolic blood pressure (BP) with absolute systolic BP < 100 mmHg, or
  - > 20 mmHg decrease in systolic BP with clinical symptoms, or
  - absolute diastolic BP < 60 mmHg
- Significant elevation of serum tryptase concentration is defined as an increase of (1.2 × baseline value) + 2
- Any Grade 2 or higher AE occurring between start of dose administration and the end of the post-dose observation period on any given treatment day
- Any Grade 2 or higher AE considered by the investigator to be related to the investigational product
- Any Grade 2 or higher local reactogenic AE (injection site pain, erythema, induration)
- Any Grade 2 or higher systemic reactogenic AEs (fever, myalgia, headache)

5. Statistical Considerations

The statistical analyses will be reported using summary tables and data listings. Numbering for the displays will be based on the recommended numbering convention provided by the International Conference on Harmonization (ICH).

5.1. Determination of Sample Size

No sample size calculations will be performed. However, the number of subjects enrolled in each study part should be adequate to meet the safety objectives and to provide preliminary evidence of efficacy.

5.2. Inferential and Descriptive Statistics

No formal inferential statistical analyses will be performed. Descriptive statistics for continuous variables will include number of subjects, mean, standard deviation, median, minimum, and maximum. Counts and percentages will be provided for categorical/ordinal variables. Unless specified in a display footnote, denominators for percentages will only consider the number of subjects being summarized or the number of non-missing responses being summarized, as appropriate. Conversion factors that may be used are as follows: 1 C = 33.8 F; 1 in = 2.54 cm; 1 kg = 2.2 lb; 1 month = 30.4375 days; 1 year = 365.25 days. The number of decimal places shown in displays will follow as closely as possible the below convention:

Statistic	Decimal Places *
n	0
Mean	1 more than Min, Max
Standard Deviation	2 more than Min, Max
Median	1 more than Min, Max
Min, Max	Same as most common in data
Percent	1

* May be limited to less than stated as space provides

Tables will be summarized for scheduled visits unless stated otherwise in this SAP, and listings will be provided for data collected via the electronic data capture (EDC) system and from external vendor(s). If date of assessment, collection, measurement, and the like is not available, then date of visit will be used if available, where applicable. If there are multiple readings taken per visit, the most recent reading from that visit will be used in summaries, unless there are pre-dose and post-dose readings taken at the same visit, as mentioned elsewhere in this SAP.

The analyses described in this plan are considered *a priori*, in that they have been defined prior to database lock. Any analysis added after the database lock will be considered post hoc and exploratory. Post hoc analyses will be labeled as such on the displays.

5.3. Multiplicity/Multiple Comparisons

There are no inferential statistical analyses planned for this study, and therefore, there are no multiplicity concerns.

5.4. Covariate Adjustments and Multicenter Analysis

No covariate analyses will be performed. No multicenter analyses will be performed.

5.5. Definition of Baseline and Treatment Groups

Baseline is defined as the most recent non-missing value obtained prior to first injection of study treatment. Summaries will be provided for the following groups, unless limited to a subset of these groups elsewhere in this SAP:

- Part 1
- Part 2
  - Cohort 1
  - Cohort 2
  - Cohort 4
  - Cohort 4 Expansion
  - Cohort 5
  - Cohort 5 Expansion
  - Overall (i.e., Part 2 Total, Displayed Total, or Expansion Total)

No other group or subgroup analyses will be performed.

5.6. Handling Dropouts and Missing Data

Unless described otherwise in other sections of this SAP, analyses will be carried out with the data available using no imputation for missing data.

5.7. Statistical Programming

All analyses, tabulations, and validation programming will be performed using SAS version 9.4 or higher. Tables and listings will be presented in PDF format. SDTM datasets will be produced using Version 3.3 of the SDTM Implementation Guide. ADaM datasets will be produced using Version 1.1 of the ADaM Implementation Guide.

SDTM, ADaM, and tables will be validated by an independent programmer. The validation process will be used to confirm that statistically valid methods have been implemented and that all data manipulations and calculations are accurate. Checks will

be made to ensure accuracy, consistency with this SAP, consistency within tables, and consistency between tables and corresponding listings.

5.8. Coding Dictionaries

Medical Dictionary for Regulatory Activities (MedDRA) version 24.1 will be used for coding adverse events and medical history excluding prior BCC treatment, procedures, and surgeries. World Health Organization (WHO) Drug Global B3 September 1, 2021 will be used for coding prior BCC medications and prior and concomitant medications. Dictionary up-versioning, if any, will be based on the most recently signed Data Management Plan (DMP).

5.9. Data Monitoring and Safety Review

AEs, SAEs, DLTs, or TRAEs SI determined by the Investigator to be related to VP-315 administration should be reviewed by the SRC for each cohort initiated. The SRC should evaluate the adverse events for any safety implications of VP-315 and make recommendations regarding subsequent enrollment and dosing. Subjects experiencing a DLT or TRAE SI are to be discontinued from treatment per Section 10.2 of the protocol.

6. Analysis Populations

Enrolled Subjects: Enrolled subjects are subjects who signed the informed consent form and were not screen failed. Enrolled subjects will serve as the population for certain analyses as described in this SAP.

Safety (SAF) Population: The Safety Population will include all subjects who received at least one injection of VP-315. The SAF Population will serve as the primary population for the analysis of safety-related data.

Full Analysis (FA) Population: The Full Analysis Population will include enrolled subjects who received one full dose (actual equals expected for at least one treated lesion) of VP-315 (for Part 1 and Part 2 Cohorts 4 and 5, a full dose consists of two injections) and have at least one non-missing post-baseline efficacy observation for histologic clearance of lesions at excision (see Section 8 of this SAP for details). The FA Population will serve as the primary population for the analysis of efficacy-related data.

Per-protocol (PP) Population: The Per-protocol Population will include FA subjects who have no major protocol deviations that may substantially affect the results of the efficacy analyses outlined in Section 8 of this SAP. The final determination on protocol violations, and thereby the composition of the PP, will be made before database lock.

The PP Population will be used as the secondary population for the efficacy analyses outlined in Section 8 of this SAP.

A non-exhaustive list of potential major protocol deviations is provided below:

- Investigational Product Deviations
  - Subject received wrong treatment
  - Deviation in IP storage
  - Error in IP dosing
- Enrollment Deviations
  - Subject is enrolled prior to determining whether eligible for study
  - Ineligible subject is enrolled
  - Enrollment occurs outside protocol window
- Study Data and/or Forms Deviations
  - Forms or data not sent from clinical site to coordinating center
  - Missing data and/or form
  - Missing images and/or operative reports
- Subject Deviations
  - Subject administration of a prohibited medication
  - Subject compliance with protocol
  - Subject met withdrawal criteria but was not withdrawn
- Visit/Procedure Schedule Deviations
  - Visit/Procedure not completed
  - Visit/Procedure not completed in window

Pharmacokinetic (PK) Population: The Pharmacokinetic Population will include SAF subjects who have at least one non-missing quantifiable observation (i.e., numeric) for LTX-315 (i.e., VP-315) concentration. Blood samples for PK assessments will only be collected for a subset of subjects in Part 2 Expansion Cohorts 4 and 5. The PK Population will be used for PK analyses.

Non-missing observations outside the limits of quantitation for LTX-315 concentration will be handled as follows:

- Observations < lower limit of quantitation (LLQ) will be assessed at 0.5 × LLQ
- Observations > upper limit of quantitation (ULQ) will be assessed at ULQ

7. Population Analysis

The conventions of Section 5 of this SAP will be applied. Tables and figures will be prefixed with 14, and listings will be prefixed 16. Tables will be provided for Part 1 and Part 2 unless noted otherwise.

7.1.1. Subject Disposition

A summary of subject disposition will be provided using enrolled subjects. The number and percentage of subjects who were enrolled, completed the study, and are included in the Safety, Full Analysis, Per Protocol, and PK Populations will be summarized, along with the reason for exclusion from the Safety, Full Analysis, Per Protocol, and PK Populations. The number and percentage of subjects discontinuing from study, and the primary reason for discontinuation from study, will also be included in the summary.

Separate listings will be provided for the following using all subjects including screen failures:

- Informed Consent (Was Subject Reconsented (Yes, No), Date of Consent/Reconsent, Date of Advarra ICF IRB Approved Version, Protocol Version Number, Version of Consent Signed (Part 1)),
- Inclusion/Exclusion (Subject Enrolled in Study (Yes, No), Enrollment Date, Part (Part 1, Part 2), Cohort (Cohort 1, Cohort 2, Cohort 4, Cohort 4 Expansion, Cohort 5, Cohort 5 Expansion), Subject Current Screen Failure (Yes, No), Subject Previous Screen Failure (Yes, No), Previous Subject ID, category/label and text for each Inclusion Criterion Not Met and each Exclusion Criterion Met for current or previous screen failure, Screen Fail Reason for current or previous screen failure), and
- Subject Visits (Visit, Date of Visit, whether Not Done, and Reason Not Done).

Separate listings will be provided for the following using enrolled subjects:

- Analysis Populations (Yes/No for Subject Inclusion in Each Population),
- End of Treatment Surgical Excision (Date Assessment Performed, All Lesions Surgically Excised (Yes, No) with Specified Reason, if applicable, Other Assessments Performed (Yes, No) with Specified Assessments, if applicable),
- End of Study Suture Removal and Post-surgical Assessment (Visit, Sutures Removed (Yes, No), Post-surgical Assessment Performed (Yes, No), Date Assessment Performed, Clinically Significant Findings (Yes, No)),

- Follow-up Call (Date of Visit, Ongoing Adverse Event Since End of Study (Yes, No), Subject Died Since Last Visit (Yes, No), Date of Death, Cause of Death (Adverse Event, Other)), and
- Subject Disposition (Enrollment Date, Date of Last Dose of Study Treatment, Date of Discontinuation or Completion of Study, Study Treatment Discontinuation and Study Discontinuation Statuses and Reasons, Date of Last Contact, and Date and Cause of Death).

7.1.2. Treatment Termination

A summary of treatment termination will be provided for TL1 and TL2 using the safety population.

Descriptive statistics will be provided for the following parameters:

- Days to Necrosis where Days to Necrosis = Earliest Date of Necrosis of Lesion Specified – Treatment Start Date.
- Total Dose to Necrosis (mg) where Total Dose to Necrosis = Sum of all Actual Injection Doses (mg) including Treatment Start Date up to but not including Earliest Date of Necrosis of Lesion Specified.

Necrosed lesions are defined as treated lesions recorded in EDC as necrosed during scheduled and unscheduled Study Treatment Administration visits.

The number and percentage of subjects will be provided for the following parameters:

- Treatment Administered
- Treatment Not Applicable (TL2 only)
- Completed Treatment
- Lesion Not Necrosed
- Lesion Necrosed
- Treatment Discontinued
- Reason for Treatment Discontinuation (Adverse Event, Withdrawal of Consent, Lost to Follow-up, Death, Pregnancy, Subject Noncompliance, Sponsor Terminated Study, Investigator Decision, Other)

- Reason for Treatment Non-administration (Adverse Event, Withdrawal of Consent, Lost to Follow-up, Death, Pregnancy, Subject Noncompliance, Sponsor Terminated Study, Investigator Decision, Other) (TL2 only)

A separate listing will be provided for Treatment Termination using the Safety Population, and the listing will include TL1 Treated (Yes, No), Date of Last TL1 Treatment, Reason TL1 Treatment Not Done or Terminated (Adverse Event, Withdrawal of Consent, Lost to Follow-up, Death, Pregnancy, Subject Noncompliance, Completed Treatment, Sponsor Terminated Study, Investigator Decision, Other) with Specified Reason, TL2 Treated (Yes, No, Not Applicable), Date of Last TL2 Treatment, and Reason TL2 Treatment Not Done or Terminated (Adverse Event, Withdrawal of Consent, Lost to Follow-up, Death, Pregnancy, Subject Noncompliance, Completed Treatment, Sponsor Terminated Study, Investigator Decision, Other) with Specified Reason.

7.2. Protocol Deviations

Protocol deviations will be collected throughout the duration of the study. Protocol deviations will be assigned a sponsor-defined category and subcategory, and each deviation will be classified by the sponsor as major or minor.

A summary of Protocol Deviations will be provided using enrolled subjects. The total number of subject-level deviations, major and minor, number and percentage of subjects with at least one deviation, major and minor, and the number and percentage of subjects with at least one deviation categorized by category and subcategory will be included in the summary. Subjects having more than one deviation may appear in more than one category or subcategory but will be counted at most once per each category and subcategory. Category and subcategory will be displayed in order of decreasing frequency of total category count, followed by decreasing frequency of total subcategory count, and then alphabetically if tied.

A separate listing will be provided for Protocol Deviations using all subjects, and the listing will include Category (Eligibility Criteria, Informed Consent, Protocol Implementation, Safety, and possibly others), Subcategory (Laboratory Tests Not Done, Missed Assessment, Participant Does Not Meet Eligibility Criteria, Participant Received Wrong Treatment, Participant Seen Outside of Visit Window, and possibly others), Deviation Issue, Date of Issue, Date Issue Identified, and Classification (Major, Minor).

Site-level deviations will not be summarized or listed. Site-level deviations may be presented in the Clinical Study Report (CSR).

7.3. Demographics and Baseline Characteristics

A summary of Demographics and Baseline Characteristics will be provided for enrolled subjects and for the analysis populations listed in Section 6 of this SAP. Baseline values will be used in summaries of parameters collected at multiple visits.

Descriptive statistics will be provided for the following parameters:

- Age (years),
- Height (cm),
- Weight (kg),
- Body Mass Index (BMI) (kg/m2),
- Serum Tryptase (ug/L),
- Total Number of Clinically Diagnosed BCC Lesions where a Clinically Diagnosed BCC Lesion means any reported lesion with a non-missing date of clinical diagnosis of BCC,
- Total Number of Pathology Diagnosed BCC Lesions where a Pathology Diagnosed BCC Lesion means any reported lesion with a non-missing date of dermatopathology diagnosis of BCC,
- Smallest Lesion Diameter Before Biopsy (cm),
- Largest Lesion Diameter Before Biopsy (cm), and
- Duration of Disease (months) where Duration of Disease = (Treatment Start Date – Earliest Date of Dermatopathology Diagnosis of BCC) / 30.4375.

The number and percentage of subjects will be provided for the following parameters:

- Sex (Male, Female),
- Female Childbearing Potential (Yes, No),
- Race (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, Mixed Race, Unknown or Not Reported),
- Ethnicity (Hispanic, Not Hispanic, Unknown or Not Reported),
- Fitzpatrick Skin Type (I-VI),
- Histologic Diagnosis at Screening (Micronodular, Nodular, Superficial) for TL1, TL2, NTL1, NTL2, NTL3, and

- BCC Location at Screening (Face or Neck, Clavicle or Shoulder, Arm, Chest or Abdomen, Back, Buttocks or Groin, Leg or Foot) for TL1, TL2, NTL1, NTL2, NTL3.

Separate listings using enrolled subjects will be provided for the following:

- Demographics and Baseline Characteristics (Age, Sex, Female Childbearing Potential, Race, Ethnicity, Height, Weight, BMI, Fitzpatrick Skin Type, Duration of Disease),
- Screening Clinical Evaluation (Lesion Number, Lesion Diameter (cm), Location, Date of Clinical Diagnosis, Date of Dermatopathology Diagnosis, Histologic Diagnosis),
- Screening Biopsy (Lesion Number, Biopsy Performed (Yes, No), Visit, Biopsy Date, Timing of Biopsy (Historical, At screening), Biopsy Type (Punch, Shave), Size of Punch Biopsy (2mm, 3mm, Other), Biopsy Sutures Removed (Yes, No), Date Biopsy Sutures Removed), and
- Biopsy Results (Lesion Number, Visit, Biopsy Date, Biopsy Type (Punch, Shave), Location, Date of Review, Histologic Diagnosis, Specimen Gross Description).

7.4. Prior and Concomitant Medications

Summaries of (a) Prior Basal Cell Carcinoma Medications using the safety population, (b) Prior Medications Excluding Prior Basal Cell Carcinoma Medications using the safety population, and (c) Concomitant Medications using the full analysis population will be provided.

For each summary, the total number of medications, the number and percentage of subjects with at least one medication, and the number and percentage of subjects with at least one medication categorized by Anatomical Therapeutic Chemical (ATC) Classification (ATCC) and Preferred Name (PN) will be provided. ATC Level 4 will be displayed, but if not available, the nearest available parental ATC Level will be displayed. Subjects having more than one medication may appear in more than one ATCC or PN but will be counted at most once per each ATCC and PN. ATCC and PN will be displayed in order of decreasing frequency of total ATCC count, followed by decreasing frequency of total PN count, and then alphabetically if tied.

Prior medications are defined as medications recorded in EDC as pre-study medications. Concomitant medications are defined as medications that are not recorded in EDC as pre-study medications, as well as medications with unknown or undeterminable start dates.

Separate listings will be provided for the following using the safety analysis population:

- Prior Basal Cell Carcinoma Medications (Medications to Report (Yes, No), Prior Therapy, Total Daily Dose, Dose Unit, Frequency, Route, Start Date, End Date), and
- Prior and Concomitant Medications Excluding Prior Basal Cell Carcinoma Medications (Medications to Report (Yes, No), Medication/Therapy, Indication, Dose, Dose Unit, Frequency, Route, Prior or Concomitant, Start Date, End Date (or Ongoing at the End of Study), whether Medication Treated an Adverse Event (Yes, No)).

7.5. Medical History

Summaries of (a) Prior Basal Cell Carcinoma Treatment, Procedures, and Surgeries and (b) Medical History Excluding Prior Basal Cell Carcinoma Treatment, Procedures, and Surgeries will be provided using the safety population.

For the Medical History Excluding Prior Basal Cell Carcinoma Treatment, Procedures, and Surgeries summary, the total number of events, the number and percentage of subjects with at least one event, and the number and percentage of subjects with at least one event categorized by system organ class (SOC) and preferred term (PT) will be provided. Subjects having more than one event may appear in more than one SOC or PT but will be counted at most once per each SOC and PT. SOC and PT will be displayed in order of decreasing frequency of total SOC count, followed by decreasing frequency of total PT count, and then alphabetically if tied.

For the Prior Basal Cell Carcinoma Treatment, Procedures, and Surgeries summary, the total number of events, the number and percentage of subjects with at least one event, and the number and percentage of subjects with at least one event categorized by Reported Term (RT) (Curettage, Electrodessication, Excision, MOHS, Topical Treatment, Other), will be provided. Subjects having more than one event may appear in more than one RT but will be counted at most once per each RT. RT will be displayed in order of decreasing frequency of total RT count, and then alphabetically if tied.

Separate listings using the safety population will be provided for the following:

- Prior Basal Cell Carcinoma Treatment, Procedures, and Surgeries (Prior Events to Report (Yes, No), Previous Treatment Received (Curettage, Electrodessication, Excision, MOHS, Topical Treatment, Other), Most Recent Treatment Received, Date of Most Recent Treatment), and

- Medical History Excluding Prior Basal Cell Carcinoma Treatment, Procedures, and Surgeries (Any Relevant Medical or Surgical History (Yes, No), Diagnosis, Condition or Surgery, Onset Date, Resolution Date (or Ongoing)).

7.6. Administration of Study Treatment

A summary of Administration of Study Treatment will be provided using the safety population.

Descriptive statistics will be provided for the following parameters:

- Total Daily Target Volume (cc),
- Total Daily Target Dose (mg),

And for each injection (Injection 1, Injection 2) within each lesion (TL1, TL2):

- Expected Injection Volume (cc),
- Actual Injection Volume (cc),
- Expected Injection Dose (mg), and
- Actual Injection Dose (mg).

The number and percentage of subjects will be provided for the following parameters:

- Study Drug Reconstituted (Yes, No).

The summary will present injection (Injection 1, Injection 2) within lesion (TL1, TL2) within scheduled visit (W1D1, W1D2, W1D3, W2D1, W2D2, W2D3).

A separate listing will be provided using the safety population for the Administration of Study Treatment, and the listing will include the parameters described as above, as well as the following parameters (not all parameters were collected at all visits):

- Lesion (to be) Injected,
- Lesion Necrosed (Yes, No, Not Applicable),
- Injection Number (1, 2),
- Injection Administered (Yes, No),
- Reason Injection Not Administered (Adverse Event, Drug Permanently Withdrawn, Investigator Decision, Subject Declined, Other),

- Received Full Dose (Yes, No),
- Dose Received if Not Full Dose,
- Reason Full Dose Not Received (Adverse Event, Drug Permanently Withdrawn, Investigator Decision, Subject Declined, Other), and
- Visit, and Date and Time of Injection.

8. Efficacy Analysis

The conventions of Section 5 of this SAP will be applied. Tables and figures will be prefixed with 14, and listings will be prefixed 16. Tables will be provided for Part 1 and Part 2 unless noted otherwise.

Each subject can have at most two distinct target lesions (TL1, TL2) and at most three distinct non-target lesions (NTL1, NTL2, NTL3). All subjects are to have TL1, but not every subject will have additional lesions. The efficacy table summaries will be provided by subject lesion.

8.1. Histologic Clearance of Treated Lesions at Excision

Histologic clearance means no residual tumor seen on dermatopathological inspection, i.e., the estimate of viable tumor within estimated volume of the entire tumor bed provided by the dermatopathologist and captured in EDC is zero. When the estimated remaining tumor volume is zero, the histologic diagnosis should be scar.

A summary of histologic clearance will be provided using the histologic diagnosis of excised treated lesions (TL1, TL2) from the end-of-treatment (EOT) visit. The histologic diagnosis categories are as follows:

- Micronodular
- Nodular
- Superficial
- Superficial and Nodular
- Scar

The summary will use the full analysis population, and for each treated lesion, the number and percentage of subjects falling into each histologic diagnosis category will be provided in the summary. The summary will also be run using the per-protocol population as outlined in Section 6 of this SAP.

A separate listing will also be provided for the Excision of all lesions (TL1, TL2, NTL1, NTL2, NTL3) using the enrolled subjects, and this listing will include Lesion Number, Visit, Excision Date, Location, Histologic Diagnosis, Date of Review, Estimate of Remaining Tumor Volume, and Specimen Gross Description.

8.2. Clinical Clearance of Treated Lesions at Excision

Clinical clearance means no residual tumor seen on clinical visual inspection.

A summary of clinical clearance will be provided using the Physician Global Assessment (PGA) of treated lesions (TL1, TL2) at the EOT visit. The PGA is an assessment of improvement that occurs post-baseline, where reported values were to be reported as change since pre-treatment. Due to the nature of the EDC form, some reported values may be reported as change since previous visit. As it is not possible to distinguish with 100% accuracy whether the reported changes were from pre-treatment or previous visit, the PGA data will be summarized as reported. The PGA categories are as follows:

- 100% Improvement, No Visible Tumor
- 75% to < 100% Improvement
- 50% to < 75% Improvement
- 25% to < 50% Improvement
- Up to 25% Improvement
- No Change
- Worse
- Not Applicable

The summary will use the full analysis population, and for each treated lesion, the number and percentage of subjects falling into each PGA category will be provided in the summary. The summary will also be run using the per-protocol population as outlined in Section 6 of this SAP.

A separate listing will also be provided for the PGA of all lesions (TL1, TL2, NTL1, NTL2, NTL3) using the enrolled subjects, and this listing will include whether a PGA was Performed (Yes, No), Visit, Date Assessment Performed, and lesion assessments per the PGA categories as described above.

8.3. Estimate of Remaining Tumor Volume and Reduction in Tumor Volume at Excision

Protocol endpoints reference that the estimated remaining tumor volume would be necrotic cells:tumor cells. However, estimated remaining tumor volume is the estimated volume of residual viable tumor cells. The assessment in the EDC is expressed as a percentage of viable tumor cells within the tumor bed which is composed of tumor cells (viable and necrotic), fibrosis, and inflammation.

A summary of the estimated remaining tumor volume (0 = None Remaining to 100 = All Remaining) will be provided using descriptive statistics for excised lesions (TL1, TL2, NTL1, NTL2, NTL3) from the end-of-treatment (EOT) visit. A 95% confidence interval for the mean estimated remaining tumor volume will also be provided in the summary using a one sample, two-sided t-test. Summary measures will be repeated for reduction in tumor volume (0 = No reduction to 100 = None Remaining).

The summaries will use the full analysis population, and for each lesion, descriptive statistics will be provided in the summary. The summaries will also be run using the per-protocol population as outlined in Section 6 of this SAP.

A separate listing will be provided for the excision of all lesions as described in Section 8.1 of this SAP.

8.4. Abscopal Effect Based on Non-treated Lesions at Excision

An abscopal effect is a phenomenon whereby the treatment of target lesions leads to improvement in both treated and non-treated lesions.

A summary of (a) histologic clearance and (b) clinical clearance for non-treated lesions will be provided to investigate a possible abscopal effect using EOT data and the full analysis population.

The histologic clearance will follow Section 8.1 of this SAP except for using the histologic diagnosis of excised non-treated lesions (NTL1, NTL2, NTL3), and the clinical clearance will follow Section 8.2 of this SAP except for using the PGA of non-treated lesions (NTL1, NTL2, NTL3). The summary will be provided by clearance (Histologic, Clinical) within lesion (NTL1, NTL2, NTL3). The summary will also be run using the per-protocol population as outlined in Section 6 of this SAP.

A separate listing will be provided for the excision of all lesions as described in Section 8.1 of this SAP, and a separate listing will be provided for the PGA of all lesions as described in Section 8.2 of this SAP.

8.5. Physician Global Assessment

The PGA is an assessment of improvement as described in Section 8.2 of this SAP.

A summary will be provided by scheduled visit (W1D2, W1D3, W1 Safety Assessment, W2D1, W2D2, W2D3, W2 Safety Assessment, EOT, EOS 1 Week Post-excision, EOS 2 Weeks Post-excision) within lesion (TL1, TL2, NTL1, NTL2, NTL3).

The summary will use the full analysis population, and for each lesion, the number and percentage of subjects falling into each PGA category will be provided in the summary. The summary will also be run using the per-protocol population as outlined in Section 6 of this SAP.

A separate listing will be provided for the PGA of all lesions as described in Section 8.2 of this SAP.

8.6. Complete Clearance of Treated Lesions at Excision

Complete clearance occurs when histologic clearance, as defined in Section 8.1 of this SAP, and clinical clearance, as defined in Section 8.2 of this SAP, are both achieved.

A summary of complete clearance will be provided using histologic clearance and clinical clearance of excised treated lesions (TL1, TL2) from the end-of-treatment (EOT) visit. The clearance categories are as follows:

- Histologic Clearance (i.e., Scar) and Clinical Clearance (i.e., 100% Improvement, No Visible Tumor)
- Histologic Clearance and Not Clinical Clearance
- Not Histologic Clearance and Clinical Clearance
- Not Histologic Clearance and Not Clinical Clearance

The summary will use the full analysis population, and for each treated lesion, the number and percentage of subjects falling into each clearance category will be provided in the summary. The summary will also be run using the per-protocol population as outlined in Section 6 of this SAP.

A separate listing will be provided for the excision of all lesions as described in Section 8.1 of this SAP, and a separate listing will be provided for the PGA of all lesions as described in Section 8.2 of this SAP.

Part 2 Cohort 4, Cohort 4 Expansion, Cohort 5, Cohort 5 Expansion, and overall (Cohorts 4 and 5 and Expansion Cohorts 4 and 5, i.e., Displayed Total) will be summarized in one display; Part 1, all Part 2 cohorts, and overall (Part 2 Total) will be summarized in another display.

8.7. Sensitivity Analysis

If the estimated remaining tumor volume or its related histologic diagnosis at EOT is missing for any subject lesion where a screening biopsy was performed, a sensitivity analysis will be provided using the full analysis population.

The overall maximum non-missing estimated remaining tumor volume (worst case reported across all subjects and lesions) and its related histologic diagnosis at EOT will be determined. All missing values for estimated remaining tumor volumes and histologic diagnoses at EOT will be set to the determined values mentioned previously in this section of the SAP, and two summaries with all parts/cohorts, one from Section 8.3 and one from Section 8.6 of this SAP, will then be rerun to explore sensitivity.

9. Safety Analysis

The conventions of Section 5 of this SAP will be applied. Tables and figures will be prefixed with 14, and listings will be prefixed 16. Tables will be provided for Part 1 and Part 2 unless noted otherwise.

9.1. Adverse Events

Adverse event (AE) summaries will be based on treatment-emergent adverse events (TEAEs). TEAEs are defined as AEs that started or worsened upon or after study treatment initiation. If it cannot be determined whether an AE is treatment emergent due to an incomplete or missing onset date and/or time, the AE will be considered treatment emergent. All AEs will be summarized using the safety population.

For AEs that are cutaneous injection site reactions (Erythema, Induration, Swelling, Blister Formation/Vesicles, Desquamation/Exfoliation, Erosion, Ulceration, Necrosis), severity was intended to be assessed on a cutaneous reaction assessment (CRA) grading scale (None (1), Mild (2), Moderate (3), Severe (4), Not Applicable (5)) and for all other AEs, severity was intended to be assessed according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 grading scale (Mild (1), Moderate (2), Severe (3), Life-threatening (4), Fatal (5)).

As the actual AE grading scale used was not captured in EDC, and the meaning of the grades is different across scales, the Maximum Severity and Grade >= 2 summaries will

be split into two sets, one for AEs that are cutaneous injection site reactions and one for AEs that are not cutaneous injection site reactions. For cutaneous injection site reactions, the preferred terms (PTs) that will be used are as follows: Injection site erythema, Injection site induration, Injection site swelling, Injection site vesicles, Injection site exfoliation, Injection site erosion, Injection site ulcer, Injection site necrosis.

An overall summary of adverse events will be provided where the number of TEAEs and the number and percent of each of the following items will be displayed.

- Subjects with at least one:
  - TEAE
  - TEAE by Strongest Relationship to Study Treatment (Not Related, Related)
  - TEAE Excluding Cutaneous Injection Site Reactions by Maximum Severity (Mild, Moderate, Severe, Life-threatening, Fatal)
  - TEAE of Only Cutaneous Injection Site Reactions by Maximum Severity (Mild, Moderate, Severe)
  - Grade >=2 Events Excluding Cutaneous Injection Site Reactions:
    - TEAE
    - TEAE by Strongest Relationship to Study Treatment
    - TEAE Occurring upon Study Treatment through Observation Period (explained in detail below)
    - TEAE with Local Reactogenicity (Injection site pain)
    - TEAE with Systemic Reactogenicity (Fever, Myalgia, Headache)
  - Severity >= Moderate Events of Only Cutaneous Injection Site Reactions (excluding Severity = Not Applicable):
    - TEAE
    - TEAE by Strongest Relationship to Study Treatment
    - TEAE Occurring upon Study Treatment through Observation Period
    - TEAE with Local Reactogenicity (Injection site erythema, Injection site induration)
  - Serious TEAE
  - DLT - Part 1 Only
  - TRAE SI - Part 2 Only
  - TEAE Leading to Study Treatment Discontinuation

- TEAE Leading to Study Discontinuation
- TEAE Leading to Death

Categories for Relationship to Study Treatment are Related and Not Related, and categories for Severity are Mild, Moderate, and Severe where the severe category will include severity levels of severe, life-threatening, and fatal as applicable.

Summaries of DLT events, TRAE SI events, and TEAEs for a subject Occurring upon Study Treatment through its Observation Period (e.g. during the DLT observation period or TRAE SI observation period) are TEAEs that a subject experiences on any day on which treatment occurs. This definition of the DLT and TRAE SI observation periods deviates from the protocol as described in section 14.

In addition, for each of the nineteen listed item mentioned previously in this section of the SAP, summaries for the total number of TEAEs, the number and percentage of subjects with at least one TEAE, and the number and percentage of subjects with at least one TEAE categorized by system organ class (SOC) and PT will be provided. Subjects having more than one AE may appear in more than one SOC or PT but will be counted at most once per each SOC and PT. For maximum severity, subjects will be counted at the most extreme category among the mild, moderate, and severe categories. For relationship to study treatment, subjects will be counted at the most related category among the unrelated and related categories. SOC and PT will be displayed in order of decreasing frequency of total SOC count, followed by decreasing frequency of total PT count, and then alphabetically if tied.

Local reactogenicity is defined as the following events: Injection site pain, Erythema, Induration. For local reactogenicity, the PTs that will be used are as follows: Injection Site Pain, Injection Site Erythema, Injection Site Induration. Systemic reactogenicity is defined as the following events: Fever, Myalgia, Headache. For systemic reactogenicity, the PTs that will be used are as follows: Fever, Myalgia, Headache.

A separate listing will be provided for all AEs using the safety population, and the listing will include the following:

- Subject Experience any Adverse Events (Yes, No),
- Adverse Event,
- TEAE (Yes, No),
- DLT (Part 1) or TEAE SI (Part 2) (Yes, No),
- Start Date and End Date (or Ongoing),

- Severity (Mild, Moderate, Severe, Life-threatening, Death),
- Serious (Yes, No),
- Relatedness (Related, Not Related),
- Action Taken (No Action Taken, Dose Reduced, Dose Interrupted, Drug Withdrawn, Not Applicable),
- Outcome (Resolved/Recovered, Resolved/Recovered with Sequelae, Not Resolved/Not Recovered, Resolving/Recovering, Fatal, Unknown),
- Related to Screening (Yes, No), and
- Screening Assessment if Related to Screening.

Additionally, a separate listing will be provided for all SAEs using the safety population, and the listing will include the following:

- Serious Adverse Event,
- Start Date and End Date (or Ongoing) where End Date (or Ongoing) is taken from reported AEs,
- Report Version (Initial, Follow-up, Final),
- Reason for Reporting (Resulted in Death, Life-threatening, Required Prolonged Hospitalization, Persistent or Significant Disability, Congenital Anomaly/Birth Defect, Important Medical Event),
- Death Date,
- Hospitalization Date,
- Autopsy (Yes, No),
- Death Certificate (Yes, No),
- Date Event Became Serious, and
- Date Event Became Non-serious.

9.2. Clinical Laboratories

Summaries of (a) serum chemistry, (b) hematology, and (c) serum tryptase will be provided using descriptive statistics and the safety population. Any clinically significant post-baseline laboratory result is to be collected as an adverse event and included in the summary of adverse events.

Results for serum tryptase and for the following laboratory parameters are expected to be available for summarization using the International System of Units (i.e., standard units).

Serum Chemistry	Hematology

• Albumin
• Alkaline Phosphatase (ALP)
• Alanine Aminotransferase (ALT) (Serum Glutamic Pyruvic Transaminase (SGPT))
• Aspartate Aminotransferase (AST) (Serum Glutamic Oxaloacetic Transaminase (SGOT))
• Blood Urea Nitrogen (BUN)
• Bicarbonate
• Calcium
• Chloride
• Creatinine
• Glucose
• Lactic Dehydrogenase (LDH)
• Potassium
• Sodium
• Total Bilirubin
• Total Protein
	• Hematocrit
	• Hemoglobin
	• Mean Corpuscular Hemoglobin Concentration (MCHC)
	• Mean Corpuscular Volume (MCV)
	• Platelet Count
	• Red Blood Cell Count (RBC)
	• White Blood Cell Count (WBC) with Differential (Absolute)
	  ○ Bands
	  ○ Blasts
	  ○ Basophils
	  ○ Eosinophils
	  ○ Lymphocytes
	  ○ Monocytes
	  ○ Neutrophils

Serum chemistry and hematology summaries will present scheduled visit and include baseline (Screening, Baseline, W1 Safety Assessment, W2 Safety Assessment, EOS 1 Week Post-excision, EOS 2 Weeks Post-excision) within alphabetically ordered laboratory parameters and, for continuous parameters, include descriptive statistics for baseline and change from baseline for post-baseline visits, if possible.

The serum tryptase summary will present scheduled visit and include baseline (Screening, Baseline, W1D1, W1D2, W1D3, W2D1, W2D2, W2D3 – not all labs are collected at all scheduled visits) and include descriptive statistics for baseline and change from baseline for post-baseline visits without timepoints, if possible. If timepoint measurements occur, serum tryptase will be displayed by scheduled timepoint (Immediately after Hypersensitivity Reaction, 60-120 min after Hypersensitivity Reaction) within scheduled post-baseline visit and include (a) descriptive statistics for

baseline and change from baseline for post-baseline timepoints, if possible, and (b) the number and percent of subjects with at least one significant elevation, where significant elevation of serum tryptase is defined as a post-baseline value >= (1.2 × baseline value) + 2.

Shift tables for laboratory parameters previously listed in this section of the SAP for (a) serum chemistry and (b) hematology will be presented, if possible, at each scheduled post-baseline visit using the safety population. Abnormal/out of range laboratory values are to be flagged as either Low or High. As CTCAE grading is not provided for numerous laboratory data, shift tables to assess changes from baseline will be presented using Low, Normal, High, and Total as categories.

Separate listing will be provided for serum chemistry, hematology, and serum tryptase using the safety population, and these lab listings will include whether Collection was Performed (Yes, No), Visit, Date and Time of Collection, Result and Units using the International System of Units (i.e., standard units), Lower and Upper Reference Range Limits using the International System of Units, Reference Range Indicator (Low, Normal, High), if available, CTCAE grade, if available, Clinical Significance (NCS, CS) for abnormal results, if available, and Change from Baseline using the International System of Units. The serum tryptase listing will also include the following for post-baseline results:

- Did the subject have a hypersensitivity reaction?
- Was a blood sample collected immediately after the hypersensitivity reaction for the serum tryptase assessment collected?
- Was the second blood sample collected between 60 - 120 minutes after the hypersensitivity reaction for the serum tryptase assessment collected?

9.3. Vital Signs Including Height and Weight

Summaries for vital signs will be provided using descriptive statistics and the safety population. Vital signs include the following parameters:

- Blood Pressure, Systolic (mmHg)
- Blood Pressure, Diastolic (mmHg)
- Height (cm)
- Weight (kg)
- BMI (kg/m2)

- Heart Rate (beats/min)
- Respiratory Rate (breaths/min)
- Temperature (C)

Non-blood pressure vital signs (Height, Weight, BMI, Heart Rate, Respiratory Rate, Temperature) will be presented in one summary and blood pressure (Systolic, Diastolic) will be presented in other summaries (one each for systolic and diastolic).

Summaries will present scheduled visit and include baseline (Screening, Baseline, W1D1, W1D2, W1D3, W1 Safety Assessment, W2D1, W2D2, W2D3, W2 Safety Assessment, Limited Safety Assessment, EOT, EOS 1 Week Post-excision, EOS 2 Weeks Post-excision – not all vital signs are collected at all scheduled visits) within the parameters mentioned previously in this section of the SAP and include descriptive statistics for baseline and change from baseline for post-baseline visits, if possible.

Blood pressure is also to be measured and will be displayed by scheduled timepoint (Pre-injection, 1 Minute Post-injection, 3 Minutes Post-injection, and then 5 through 120 Minutes Post-injection in increments of 5 minutes) within injection (Injection 1, Injection 2 – not all timepoints are collected for all injections) within scheduled visit and include descriptive statistics for change from pre-injection for post-injection readings on that same visit, if possible.

A summary will also be provided for the number of events, and the number and percentage of subjects with at least one event, for each of the following parameters within injection visit (W1D1, W1D2, W1D3, W2D1, W2D2, W2D3):

- 20 mmHg decrease in systolic BP with absolute systolic BP < 100 mmHg
- 20 mmHg decrease in systolic BP with clinical symptoms
- Absolute diastolic BP < 60 mmHg

Decrease in systolic BP will be determined three ways: (a) change from baseline, (b) change from pre-injection for post-injection readings on that same visit, and (c) change from the previous most recent non-missing reading on the same visit. The clinical symptoms tabulation related to a decrease in systolic BP will be determined by counting TEAEs with a start date matching the BP event date that are (a) recorded as DLTs (Part 1) or TRAEs SI (Part 2), (b) related to study treatment, and (c) have the following symptomatic events: Dizziness, Shortness of breath, Fainting, Nausea, Diaphoresis, Blurry vision, Headache, Fatigue. For symptomatic events, the PTs that will be used are

as follows: Dizziness, Dyspnoea, Syncope, Nausea, Hyperhidrosis, Vision blurred, Headache, Fatigue.

A separate listing will be provided for Vital Signs using the safety population, and this listing will include Vital Signs Collected (Yes, No), Visit, Date of Reading, Reading Value and Unit, and Change from Baseline for all parameters.

For BP collected on injection days, the listing will include BP Collected After Injection (Yes, No), Visit, Date and Time of Reading, Timepoint of Reading, Injection Number, Reading Value and Unit, Change from Baseline, Change from Pre-injection for post-injection readings on that same visit, if possible, Change from the Previous Most Recent non-missing reading on the same visit, if possible, and Reason Timepoint Not Done.

9.4. Electrocardiogram

Summaries for electrocardiogram (ECG) readings from 12-lead and Holter/telemetry 5-lead assessments will be provided using the safety population. A continuous summary and a categorical summary will be presented for the 12-lead assessments, as well as for the Holter/telemetry 5-lead assessments.

Descriptive statistics will be provided for the following parameters:

- 12-lead
  - Heart Rate (beats/min)
  - PR Interval (msec)
  - QRS Interval (msec)
  - QT Interval (msec)
  - QTc Interval (msec) (correction type not provided in data)
  - QTcB Interval (msec)
  - QTcF Interval (msec)
  - RR Interval (msec)
  - P-Axis (%)
  - R-Axis (%)
  - T-Axis (%)

- Holter/telemetry 5-lead
  - Heart Rate (beats/min)

- PR Interval (msec)
- QRS Interval (msec)
- QT Interval (msec)

The number and percentage of subjects will be provided for the following parameters:

- 12-lead
  - Modality (HeartCor, Locally)
  - Overall Assessment/Interpretation (Normal, Abnormal NCS, Abnormal CS)
  - Predominant Rhythm (Normal Sinus Rhythm, Sinus Tachycardia, Sinus Bradycardia, and possibly others)
  - Principal Investigator/Medical Doctor Notification (Yes, No)

- Holter/telemetry 5-lead
  - Predominant Rhythm (Normal Sinus Rhythm, Sinus Tachycardia, Sinus Bradycardia, and possibly others)

The Holter/telemetry 5-lead is to be monitored continuously on injection visits, with a planned start 15 minutes prior to injection and a planned continuance until after the last injection of the day. As a continuous full-length reading, there are no 5-lead baseline or pre-injection values, but the 5-lead full-length reading is to be broken where possible into sub-readings/timepoints (Holter Start, Holter Pre-injection, Holter 5 Minute Post-injection 1, Holter 15 Minute Post-injection 1, Holter 5 Minute Post-injection 2, Holter 15 Minute Post-injection 2, Holter End, and any change in BP occurring during the full-length Holter reading that would qualify as a DLT/TRAE SI (these specific changes in BP will be referred to as BP Dips below)).

Due to different sources for recorded times related to the Holter/telemetry 5-lead data, the possibility of mis-ordering timepoints based on recorded times exists; therefore, the sub-readings/timepoint labels of Holter Start and Pre-injection will be considered when determining the Baseline and Pre-injection values as follows.

The 5-lead Baseline value for use in Change from Baseline calculations will be the most recent non-missing value from the following possibilities:

- Holter Start Timepoint on Day of First Treatment Injection

- Holter Pre-injection Timepoint on Day of First Treatment Injection
- BP Dip(s) on Day of First Treatment Injection where Time of Dip(s) < Time of First Treatment Injection, and there are Holter/telemetry 5-lead data associated with these BP Dip(s)

Each subject has his or her own Baseline value per parameter, if determinable, to be used for calculating Change from Baseline.

The 5-lead Pre-injection values for use in Change from Pre-injection for Post-injection Readings on that Same Visit calculations will be the most recent non-missing values, on the Same Visit, from the following possibilities:

- Holter Start Timepoint on Day of Treatment Injection
- Holter Pre-injection Timepoint on Day of Treatment Injection
- BP Dip(s) on Day of Treatment Injection where Time of Dip(s) < Time of Treatment Injection, and there are Holter/telemetry 5-lead data associated with these BP Dip(s)

Each subject has his or her own Pre-injection value per parameter per injection visit, if determinable, to be used for calculating Change from Pre-injection for Post-injection Readings on that Same Visit.

Summaries will present scheduled visit and include baseline (Screening, W1D1, Baseline, W1D2, W1D3, W1 Safety Assessment, W2D1, W2D2, W2D3, W2 Safety Assessment, EOT – not all ECG parameters are collected at all scheduled visits) within the parameters mentioned previously in this section of the SAP and, for continuous parameters, include descriptive statistics for baseline and change from baseline for post-baseline visits, if possible.

Holter/telemetry 5-lead values will also be displayed by predetermined timepoint within scheduled visit and include descriptive statistics for change from pre-injection for post-injection readings on that same visit, if possible. Due to sparsity, the sub-reading/timepoints for any change in BP that would qualify as a DLT/TRAE SI will not be included in the summary but will be displayed in the 5-lead listings.

A separate listing will be provided for the continuous parameters from the 12-lead assessment using the safety population, and this listing will include Visit, Recording Date and Time, Heart Rate, Interval and Axis readings, and Change from Baseline.

A separate listing will also be provided for the categorical parameters from the 12-lead assessment using the safety population, and this listing will include whether the Assessment was Performed (Yes, No), Visit, Recording Date and Time, the categorical ECG parameters described above, and Abnormal Findings.

Additionally, a separate listing will also be provided for the continuous parameters from the Holter/telemetry 5-lead assessment using the safety population, and this listing will include Visit, Date of Visit, Timepoint, Time of Timepoint, Heart Rate, Interval readings, Change from Baseline, and Change from Pre-injection.

A separate listing will also be provided for the categorical parameter(s) from the Holter/telemetry 5-lead assessment using the safety population, and this listing will include Visit, Date of Visit, Timepoint, Time of Timepoint, and the categorical ECG parameter described above.

9.5. Cutaneous Reaction Assessment

A summary of the cutaneous reaction assessments (CRAs) will be provided using the safety population. The number and percentage of subjects falling into each severity category (None (1), Mild (2), Moderate (3), Severe (4), Not Applicable (5)) for reactions of Erythema, Induration, Swelling, Blister Formation, Desquamation, Erosion, Ulceration, and Necrosis will be provided in the summary.

The summary will present reaction within scheduled visit (W1D2, W1D3, W1 Safety Assessment, W2D1, W2D2, W2D3, W2 Safety Assessment, Limited Safety Assessment, EOT, EOS 1 Week Post-excision, EOS 2 Weeks Post-excision) within lesion (TL1, TL2, NTL1, NTL2, NTL3).

A separate listing will be provided for CRAs using the safety population, and this listing will include whether a CRA was Performed (Yes, No), Visit, Date Assessment Performed, and reaction assessments as described above.

A separate listing will also be provided for Photo Assessment using the safety population, and this listing will include Visit, Lesion Photos Taken (Yes, No), Date and Time of Photos, and Photos Uploaded (Yes, No).

9.6. Dermatologic and Physical Examinations

A dermatologic examination including Fitzpatrick Skin Type is to occur at screening, and a limited physical examination of the following body systems may occur at scheduled visits (Screening, W1D1, W1D2, W1D3, W1 Safety Assessment, W2D1, W2D2, W2D3,

W2 Safety Assessment, Limited Safety Assessment, EOT– not all body systems are examined at all scheduled visits) or for symptom or AE-directed reasons.

- General Appearance
- Head, Ears, Eyes, Nose, Oral, Throat
- Respiratory
- Cardiovascular
- Gastrointestinal
- Genitourinary
- Musculoskeletal
- Neurological
- Lymphatic
- Skin
- Reproductive
- Endocrine
- Other

Separate listings will be provided for Dermatologic and (Limited) Physical Examinations using the safety population. The Dermatologic Examination listing will include Exam was Performed (Yes, No), Visit, Date Exam Performed, Clinically Significant (Yes, No), Description, and Fitzpatrick Skin Type (I-VI). The (Limited) Physical Examination listing will include Exam was Performed (Yes, No), Visit, Date Exam Performed, Body System Examined, Result (Normal, Abnormal, Not Done), and Abnormal Findings.

No summary tables will be provided. Fitzpatrick Skin Type (I-VI) is summarized in the Demographics and Baseline Characteristics display described in Section 7.3 of this SAP.

9.7. Pregnancy Tests and Partner Pregnancy

Partner pregnancy is to be reported for all subjects at screening, and only females of childbearing potential are tested for pregnancy. Urine pregnancy tests are to be performed prior to W1D1 and W2D1 injections. Serum-based pregnancy tests are to be performed at other scheduled visits (Screening, W1 Safety Assessment, W2 Safety Assessment, EOS 1 Week Post-excision, EOS 2 Weeks Post-excision – not all laboratory parameters are collected at all scheduled visits).

Separate listings will be provided for Pregnancy Tests and Partner Pregnancies using the safety population. The Pregnancy Tests listing will include Visit, Test Performed (Yes, No), Date of Test, Laboratory Test Name, Test Type (Serum, Urine), and Result (Positive, Negative). The Partner Pregnancies listing will include Visit, Date of Visit, and whether Subject Shared Partner is Pregnant (Yes, No).

No summary tables will be provided.

10. Treatment Satisfaction Analysis

The conventions of Section 5 of this SAP will be applied. Tables and figures will be prefixed with 14, and listings will be prefixed 16. Tables will be provided for Part 1 and Part 2 unless noted otherwise.

10.1. SCAR-Q – Appearance Scale

A summary of SCAR-Q – Appearance will be provided using the full analysis population. Descriptive statistics will be provided for Raw Sum (12 = Best to 48 = Worst), Rescored Sum (12 = Worst to 48 = Best), and Score (0 = Worst to 100 = Best). The number and percentage of subjects falling into each scale level (1 = Not at all, 2 = A little, 3 = Quite a bit, 4 = Very much) for responses to the following twelve "How much are you bothered by..." assessment questions will be provided in the summary:

1. How your scar looks from far away
2. How wide your scar looks
3. How your scar looks from different angles
4. How thick your scar looks (more raided than you would like)
5. The length of your scar
6. The surface of your scar (more bumpy than you would like)
7. The color of your scar
8. The difference between the color of your scar and your skin color
9. The contour of your scar (not as flat as you would like)
10. The overall size of your scar
11. How your scar looks close up
12. How noticeable your scar is

Raw Sum is calculated as follows:

- If the number of missing responses is 0, then Raw Sum is the total of the numeric response values.

- If the number of missing responses is >0 and <6, then Raw Sum is [(number of missing responses · mean of non-missing response) + total of non-missing numeric response values].
- If the number of missing responses is >=6, then Raw Sum is missing.

Rescored Sum is calculated as follows:

- Each non-missing numeric response value is transformed into 5 – response value.
- Then proceed the same as for Raw Sum, except use transformed response values.

Score is calculated as follows:

- If Rescored Sum is missing, then Score is missing.
- Otherwise, Score is provided by the SCAR-Q Conversion Table.

The summary will present Raw Sum, Rescored Sum, Score, and the above listed questions within scheduled visit (W1 Safety Assessment, W2 Safety Assessment, EOT).

A separate listing will be provided for SCAR-Q – Appearance using the full analysis population, and this listing will include Visit, Date of Visit, and the parameters as described above.

Only Part 2 will be summarized.

10.2. FACE-Q – Psychological Function

A summary of FACE-Q – Psychological Function will be provided using the full analysis population. Descriptive statistics will be provided for Raw Sum (10 = Worst to 40 = Best) and Score (0 = Worst to 100 = Best). The number and percentage of subjects falling into each scale level (1 = Definitely disagree, 2 = Somewhat disagree, 3 = Somewhat agree, 4 = Definitely agree) for responses to the following ten assessment statements will be provided in the summary:

a. I like myself
b. I feel positive about myself
c. I feel okay about myself
d. I feel happy
e. I am comfortable with myself
f. I am accepting of myself

g. I feel good about myself
h. I feel confident
i. I feel attractive
j. I feel great about myself

Raw Sum is calculated as follows:

- If the number of missing responses is 0, then Raw Sum is the total of the numeric response values.
- If the number of missing responses is >0 and <5, then Raw Sum is [(number of missing responses · mean of non-missing response) + total of non-missing numeric response values].
- If the number of missing responses is >=5, then Raw Sum is missing.

Score is calculated as follows:

- If Raw Sum is missing, then Score is missing.
- Otherwise, Score is provided by the FACE-Q Conversion Table.

The summary will present Raw Sum, Score, and the above listed statements within scheduled visit (W1 Safety Assessment, W2 Safety Assessment, EOT).

A separate listing will be provided for FACE-Q – Psychological Function using the full analysis population, and this listing will include Visit, Date of Visit, and the parameters as described above.

Only Part 2 will be summarized.

10.3. Scar Assessment

A summary of the Scar Assessment will be provided using the full analysis population. The number and percentage of subjects falling into each response category for the following items will be provided in the summary:

- Subject Asked if Any Scars are Related to Study Treatment (Yes, No)
- Subject Response to Scars Inquiry (Yes, I have scar(s), No, I don't have any scar(s)):

  And for each scared lesion (TL1, TL2, NTL1, NTL2, NTL3):

- Severity of Lesion Scar (Mild, Moderate, Severe)
- Lesion is Most Bothersome to Subject (Yes, No)

The summary will present the above listed parameters within scheduled visit (W1 Safety Assessment, W2 Safety Assessment, EOT).

A separate listing will be provided for the Scar Assessment using the full analysis population, and this listing will include Visit, Date of Visit, and the parameters as described above.

Only Part 2 will be summarized.

10.4. Scar Cosmesis Assessment and Rating Scale

A summary of the Scar Cosmesis Assessment and Rating (SCAR) Scale will be provided using the full analysis population. Descriptive statistics will be provided for Sum (0 = Best to 15 = Worst) and Partial Sum (0 = Best to 13 = Worst).

Sum is to be provided in EDC when all assessment items (i.e., clinical and patient items shown below) have non-missing responses. Partial Sum is derived as the sum of non-missing responses to the clinical items (i.e., excluding the two "bothered by" patient items); if any clinical item is missing a response, then Partial Sum is derived as missing.

The number and percentage of subjects falling into each response category for the following clinical and patient items will be provided in the summary:

Clinical Items

- Scar Spread (0 = None to near-invisible; 1 = Pencil-thin line; 2 = Mild spread, noticeable on close inspection; 3 = Moderate spread, obvious scarring; 4 = Severe spread)
- Erythema (0 = None; 1 = Light pink, some telangiectasias may be present; 2 = Red, many telangiectasis may be present; 3 = Deep red or purple)
- Dyspigmentation (0 = Absent; 1 = Present)
- Track Marks or Suture Marks (0 = Absent; 1 = Present)
- Hypertrophy/Atrophy (0 = None; 1 = Mild: Palpable, barely visible hypertrophy or atrophy; 2 = Moderate: Clearly visible hypertrophy or atrophy; 3 = Severe: Marked hypertrophy or atrophy or keloid formation)
- Overall Impression (0 = Desirable scar; 1 = Undesirable scar)

Patient Items

- Subject Bothered by Any Itch from Scar (0 = No; 1 = Yes)
- Subject Bothered by Any Pain from Scar (0 = No; 1 = Yes)

The SCAR Scale scheduled visit is EOT prior to excision.

A separate listing will be provided for the SCAR Scale using the full analysis population, and this listing will include Visit, Date of Visit, and the parameters as described above.

Only Part 2 Cohort 4, Cohort 4 Expansion, Cohort 5, Cohort 5 Expansion, and overall (Cohorts 4 and 5 and Expansion Cohorts 4 and 5, i.e., Displayed Total) will be summarized.

11. Immune Response and Genomic Analyses

Analysis of multiplex immunohistochemical staining for T-cell subsets and immune activation markers in tumor tissue samples, analysis of T-cell clonality in blood and tumor tissue samples, and other genomic or immune response summaries, modeling, analyses, and graphics will be addressed by an external vendor in a separate analysis plan.

A separate listing will be provided for Plasma Immune Response Collections using enrolled subjects, and the listing will include Visit, whether the Subject Consented to Participate in the Plasma Immune Response Subgroup (Yes, No), whether the Related Sample Collected Prior to First Treatment (Yes, No), and Date and Time of Collection.

No summary tables will be provided.

12. Pharmacokinetic Analysis

PK collections are to be performed on W1D1 and W1D2. Per protocol, concentrations of LTX-315 and metabolites were to be provided, but the data will contain only LTX-315 concentrations.

Summaries of (a) PK concentrations by scheduled timepoint and (b) PK parameters will be provided using descriptive statistics and the PK population. The PK parameters will be estimated by an external vendor, as specified in a separate specification document, and may include C_{max}, T_{max}, $AUC_{0\text{-}last}$, AUC_{tau}, and/or AUC_{inf} among others. Descriptive statistics as mentioned in Section 5.2 of this SAP, as well as the coefficient of variation (%), geometric mean, and geometric coefficient of variation (%) will be provided for both PK summaries.

The scheduled timepoints are as follows:

- Pre-first W1D1 Injection: Immediately Prior
- Post-first W1D1 Injection: 2 and 5 Minutes

- Post-last W1D1 Injection: 2, 5, 10, 20, 30, 60, and 120 Minutes
- Post-last W1D1 Injection: 24 Hours – Drawn on W1D2 Prior to Injection

VP-315 metabolites, PK parameter estimates, dose proportionality, and other PK summaries, modeling, analyses, and graphics will be addressed by an external vendor in a separate analysis plan.

A separate listing will be provided for PK collections using enrolled subjects, and the listing will include whether the Subject Consented to PK Collection (Yes, No), Visit, Timepoint, whether the PK Sample was Collected (Yes, No), and Date and Time of Collection.

A separate listing will also be provided for PK concentrations of LXT-315 (i.e., VP-315) using the PK population, and this listing will include Visit, Timepoint, Analyte (LTX-315), Concentration (ng/mL), Date and Time of Collection (from PK collections data), and Sample Comments.

Additionally, a separate listing will be provided for PK parameters using the PK population, and this listing will include PK parameters provided by the external vendor.

Only Part 2 Cohort 4 Expansion, Cohort 5 Expansion, and overall (Expansion Cohorts 4 and 5, i.e., Expansion Total) will be summarized.

13. Differences Between Protocol and Statistical Analysis Plan

If there are differences between the protocol and this SAP, then this SAP takes precedence.

14. Where Statistical Analysis Plan Differs from Protocol

The following are changes in this SAP that differ from the protocol:

- In Section 2 of this SAP, Objectives and Endpoints and Section 8.3, Estimate of Remaining Tumor Volume and Reduction in Tumor Volume at Excision:
  Estimate of reduction in tumor volume (necrotic cells:tumor cells) at excision is added as an additional endpoint not included in the protocol.
- In Section 6 of this SAP, Analysis Populations:
  A definition of enrolled subjects is not included in the protocol but is included in this SAP.
- In Section 8.3 of this SAP, Estimate of Remaining Tumor Volume at Excision:

The protocol mentions that the estimated remaining tumor volume would be necrotic cells:tumor cells. However, the estimated remaining tumor volume will be provided by the dermatopathologist and captured in EDC as an estimate of viable tumor within estimated volume of the entire tumor bed expressed as a percentage.

- In Section 9.1 of this SAP, Adverse Events:
  Per protocol, the DLT observation period for Part 1 subjects is given as completing Week 1 dosing. In this SAP, to clarify that completing dosing is not necessary for observation, the DLT observation period for Part 1 subjects any day on which treatment occurs Per protocol, the TRAE SI observation period for Part 2 subjects occurs during treatment visit. In this SAP, the TRAE SI observation period for Part 2 subjects is defined as any day on which treatment occurs.
- In Section 9.2 of this SAP, Clinical Laboratories:
  As CTCAE grading is not provided for numerous laboratory data, shift tables to assess changes from baseline will be presented using Low, Normal, High, and Total as categories.
- In Section 12 of this SAP, Pharmacokinetic Analysis:
  Per protocol, concentrations of LTX-315 and metabolites were to be provided, but the data will contain only LTX-315 concentrations.

15. Minor Changes in Displays

Minor changes in display categories, minor rearrangement of display layouts, and changing single displays into multiple displays and vice versa due to spacing or presentation needs are permitted without sponsor approval.

16. References

Verrica Pharmaceuticals Inc. VP-315-201: A Phase 2, Multicenter, Open-label, Proof-of-Concept Study with Safety Run-in to Evaluate the Safety, Pharmacokinetics, and Efficacy of VP-315 in Adult Subjects with Basal Cell Carcinoma, Protocol Version 9.0 (Amendment 8). 13-Oct-2023.

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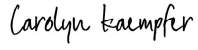
Carolyn Kaempfer carolyn.kaempfer@veristat.com Manager, Biostatistics Security Level: Email, Account Authentication (Required)	 Signature Adoption: Pre-selected Style Signature ID: 6C9CC10B-B834-4EA2-A9C1-69AA26C46E6E Using IP Address: 97.113.174.253 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I am the author of this document	Sent: 9/6/2024 6:10:58 PM Viewed: 9/6/2024 6:11:29 PM Signed: 9/6/2024 6:11:54 PM
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Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	9/6/2024 6:10:58 PM
Certified Delivered	Security Checked	9/6/2024 6:51:16 PM
Signing Complete	Security Checked	9/6/2024 6:51:51 PM
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