16.1.9 Documentation of Statistical Methods

Final Statistical Analysis Plan, Version 1.0, dated 17-Aug-2018

Statistical Analysis Plan

Sponsor	Novan, Inc.
Protocol Title:	A PHASE 2 MULTI-CENTER, RANDOMIZED, DOUBLE-BLIND, VEHICLE-CONTROLLED, ASCENDING DOSE STUDY OF SB206 IN SUBJECTS WITH MOLLUSCUM CONTAGIOSUM
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Not applicable.

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1. Overview

This statistical analysis plan (SAP) describes the planned analysis and reporting for Novan, Inc. protocol NI-MC201 (a phase 2 multi-center, randomized, double-blind, vehicle-controlled, ascending dose study of SB206 in subjects with molluscum contagiosum), version 3.0, dated 29-Jun-2018. Reference materials for this statistical plan include the protocol and the accompanying sample data collection documents. Operational aspects related to collection and timing of planned clinical assessments are not repeated in this SAP unless relevant to the planned analysis.

The structure and content of this SAP provides sufficient detail to meet the requirements identified by the Food and Drug Administration (FDA), European Medicines Agency (EMA), and International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use: Guidance on Statistical Principles in Clinical Trials[1]. All work planned and reported for this SAP will follow internationally accepted guidelines, published by the American Statistical Association[2] and the Royal Statistical Society[3], for statistical practice.

The planned analyses identified in this SAP may be included in clinical study reports (CSRs), regulatory submissions, or future manuscripts. Also, post-hoc exploratory analyses not necessarily identified in this SAP may be performed to further examine study data. Any post-hoc or unplanned, exploratory analysis presented in the CSR will be clearly identified as such in the final CSR.

The statistical plan described hereafter is an *a priori* plan. It will be submitted to the file prior to the generation of any unblinded inferential or descriptive analyses by the project statistician. To further maintain the integrity of study data, the unblinded data summaries pertaining to Novan, Inc. NI-MC201 and occurring prior to final database lock, in support of review and reporting of safety, are produced by an unblinded statistician who provided unblinded summaries for the DSMB but was otherwise not involved in the management of the study.

2. Study Objectives and Endpoints

2.1. Study Objectives

This study is being conducted to evaluate the efficacy, safety, and tolerability of SB206 for the topical treatment of MC (Molluscum Contagiosum). Results will be used to determine the dose(s) for future studies. The study objectives are as follows.

- To evaluate the efficacy of SB206 over vehicle gel for up to 12 weeks of topical treatment of MC
- To evaluate the safety and tolerability of SB206 for up to 12 weeks treatment of MC
- To evaluate and determine a safe and efficacious SB206 dose level for future studies

2.2. Study Endpoints

The following endpoints will be assessed during the study.

2.2.1. Safety Endpoints

Safety assessments will be performed at scheduled timepoints throughout the study and include physical examination, vital signs, standard clinical laboratory testing (hematology, serum chemistry), methemoglobin measurement, pregnancy test, tolerability evaluation, concomitant medications (CM), and adverse events (AEs).

2.2.2. Efficacy Endpoints

2.2.2.1. Primary Efficacy Endpoint

Proportion of subjects achieving complete clearance of all MC at Week 12 (Subjects who achieved complete clearance before Week 12 need to maintain complete clearance at Week 12)

2.2.2.2. Secondary Efficacy Endpoint(s)

- Proportion of subjects achieving complete clearance of all MC at each visit
- Time to first complete clearance of all MC
- Proportion of subjects achieving at least a 75% reduction from baseline in number of MC at each visit
- Mean change from baseline in number of MC at each visit
- Mean percent change from baseline in number of MC at each visit

2.2.2.3. Exploratory Efficacy Endpoint(s)

- Proportion of subjects whose lesion count decreases or, separately, increases from baseline at each visit
- Absolute number of subjects who show new lesions after once achieving complete clearance at each visit

2.2.3. Pharmacokinetic/Pharmacodynamic Variable(s)

PK sampling and analysis will be conducted on a subset of subjects in Cohorts 3 and 4. Descriptive results will be reported in the CSR.

3. Overall Study Design and Plan

This is a phase 2 multi-center, randomized, double-blind, vehicle-controlled ascending dose study to be conducted in up to approximately 192 or 256 non-immunocompromised subjects with MC. After obtaining informed consent, subjects who satisfy entry criteria will be randomized 3:1 (active: vehicle) to ascending, sequential dose cohorts of SB206. The highest tolerated dose will also be run in a cohort once daily. Approximately 64 subjects will be randomized to each cohort (see study schematic). At randomization, subjects will be stratified by number of lesions at Baseline (3-18; 19-70) and atopic dermatitis (AD) history (with AD history; without AD history). A maximum of 16 adult subjects, ages 18 and above, will be randomized into each cohort; the remaining subjects will be aged 2-17 years.

Subjects will be treated once daily, twice daily or three times a week for up to 12 weeks for all lesions identified at Baseline and new lesions that arise during treatment. If a subject clears all lesions (confirmed by the Investigator at the next regular scheduled visit), the treatment period will end and subjects will be followed for recurrence/new lesions until Week 12/Early Termination (ET). Subjects will visit the clinic at Screening, Baseline, Week 1, Week 2, Week 4, Week 8, and Week 12/ET.

After 30 subjects in a cohort have completed 2 weeks of treatment, the data safety monitoring board (DSMB) will review the available unblinded safety (methemoglobin, AEs, serious AEs (SAEs), lab) and tolerability data. Using predetermined criteria documented in the DSMB charter, the DSMB will determine if the data supports escalating to the next highest dose for the next cohort or if the data shows the dose is not tolerable, decreasing to the next lower dose or frequency for the next cohort. After 64 subjects are randomized to a cohort, the next cohort will be opened. Once a subject is randomized to a cohort, the subject will stay in that cohort. If a subject discontinues treatment, the subject will continue in the study and be followed until Week 12/ET unless the subject/caregiver withdraws the consent.

The standard operating procedures of the DSMB will be documented in the DSMB charter, including the board's accountability to Novan.

3.1. Overall Design

3.2. Sample Size and Power

Approximately 192 subjects, 2 years of age and older, with a minimum of 3 and a maximum of 70 lesions at baseline will be randomized across a minimum of 3 cohorts. If the third cohort is administered 12% BID then up to an additional 64 subjects will be randomized in a fourth cohort. This Phase 2 study was not powered for formal statistical comparisons. Each of the SB206 active dose groups will be compared to Vehicle gel. No adjustments will be made for multiplicity. No imputations will be utilized for safety endpoints.

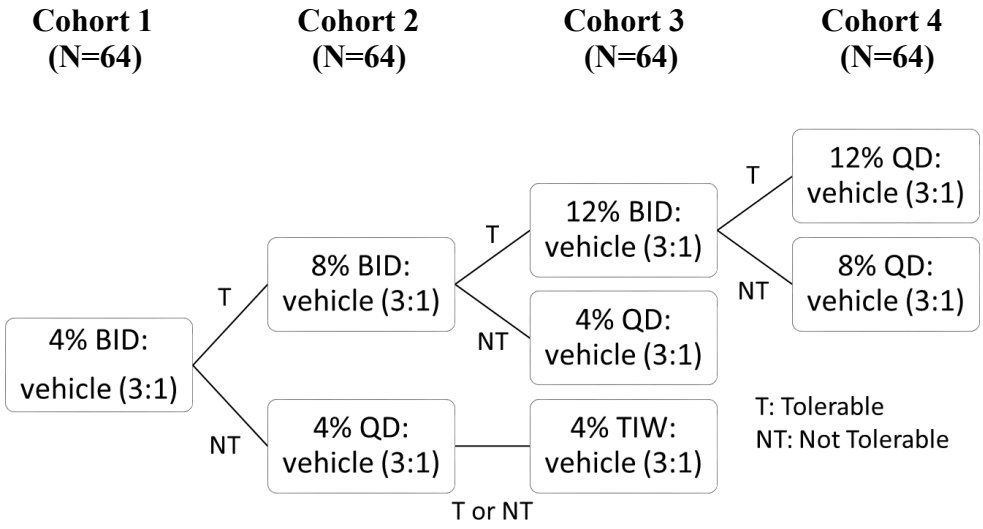
3.3. Study Population

The study population will consist of males and females, 2 years of age and older, with a minimum of 3 and a maximum of 70 MC at baseline.

3.4. Treatments Administered

Subjects will be treated once daily, twice daily, or three times a week for up to 12 weeks for all lesions identified at baseline and new lesions that arise during treatment. Subjects who satisfy entry criteria will be randomized 3:1 (active:vehicle) to ascending, sequential dose cohorts of SB206.

Figure 1: Study Schematic



Note: Tolerated (T) or not tolerated (NT) is decided on a cohort basis, not on a subject level, after 30 subjects have completed 2 weeks of treatment.

3.5. Method of Assigning Subjects to Treatment Groups

In this randomized, double-blind, vehicle-controlled study, subjects who meet study entry criteria will be randomly assigned in a 3:1 ratio (active: vehicle) to ascending, sequential dose cohorts of SB206. The randomization schedule will be computer generated using a permuted block algorithm and will randomly allocate IP to randomization numbers. The randomization numbers will be assigned sequentially through a central interactive web response system (IWRS) as subjects are entered into the study (Cohort 1, then Cohort 2, then Cohort 3, then Cohort 4). Randomization will be stratified by number of lesions at baseline (3-18, 19-70) and atopic dermatitis history (with AD history vs without AD history). A maximum of 16 adult subjects, ages 18 and above, will be randomized into each cohort.

3.6. Blinding and Unblinding

All subjects, investigators, and study personnel involved in the conduct of the study will be blinded to treatment assignment, with the exception of a specified unblinded statistician who will generate and have access to the randomization code. The unblinded study personnel will not otherwise participate in study procedures or data analysis prior to unblinding of the study data to all study related personnel.

A DSMB will conduct an unblinded review of safety and tolerability data after 30 subjects are enrolled and treated for 2 weeks within each cohort. Unblinded personnel who are not otherwise involved in the study will prepare the data for review.

Study personnel will endeavor to safeguard the integrity of the study blind to minimize bias in the conduct of the study. Unblinding of single events in support of safety reporting will not be viewed as introducing study bias and all information of treatment assignment will be limited to individuals supporting safety reporting.

3.7. Schedule of Events

A detailed schedule of events for the study is provided in Table 1.

Table 1: Schedule of Assessments

	Screening[1] (Day -28 to Day 1)	Visit 1[1] Baseline (Day 1)	Visit 2[2] Week 1 (Day 8 ±3)	Visit 3[2] Week 2 (Day 15 ±3)	Visit 4[2] Week 4 (Day 29 ±3)	Visit 5[2] Week 8 (Day 57 ±3)	Visit 6[2] Week 12/ET (Day 85 ±7)
Informed Consent (Assent)	X						
Demographics	X						
Medical and Medication History	X	X					
Lesion Counts	X	X	X	X	X	X	X
Physical Exam		X					X
Vital Signs		X	X	X	X	X	X
Chemistry & Hematology[3]		X					X
Methemoglobin[4]		X	X	X	X	X	X
Assessment of hMAP3 plasma concentration[5,6]							X
Urine Pregnancy Test[7]	X	X			X	X	X
Tolerability Evaluation		X	X	X	X	X	X
Photographs[6]		X			X		X
In Clinic Study Drug Application and Provide Subject Instructions		X					
Dispense Subject Diary		X			X	X	
Review Study Compliance			X	X	X	X	X
Collect Subject Diary					X	X	X
Drug Dispensed		X			X	X	
Collect Study Drug					X	X	X
Randomization		X					
Review Concomitant Medications and Adverse Events		X	X	X	X	X	X

[1] Screening and Baseline may occur on the same day
[2] All visit dates are in reference to Baseline, e.g. Week 1 occurs 7 days after Baseline Visit.
[3] Collected at the last day of treatment.
[4] Collected via pulse co-oximetry at site.
[5] Blood for determination of the hMAP3 plasma concentration will be collected at a single time approximately 1 to 6 hours following last dose application. The time of the sample collection and the time of last dose preceding the scheduled visit will be recorded. The blood sample may be collected at the same time as the chemistry and hematology sample.
[6] Selected sites and subjects.
[7] Females 10 years of age and older. Subjects whose Baseline visit is within 7 days of Screening do not require UPT retesting.

4. Statistical Analysis and Reporting

This SAP is based on the approved clinical study protocol, version 3.0, dated 29-Jun-2018.

This SAP addresses the safety and efficacy objectives of the study and describes the statistical methods that are to be used both for the final analysis of the completed study and the interim analysis of data through Cohort 3.

The reader of this SAP is encouraged to also read the clinical protocol, DSMB charter, and all other identified documents, for details on the planned conduct of this study. Operational aspects related to collection and timing of planned clinical assessments are not repeated in this SAP unless relevant to the planned analysis.

4.1. Introduction

Data processing, tabulation of descriptive statistics, calculation of inferential statistics, and graphical representations will be performed primarily using SAS (release 9.4 or higher). If the use of other software is warranted, the final statistical methodology report will detail what software was used for what purposes.

Continuous (quantitative) variable summaries will include the number of subjects (n) with non-missing values, mean, standard deviation (SD), median, minimum, and maximum. Other statistics such as coefficient of variation (%CV), quartiles, confidence intervals (CIs), and number of missing values may be added as appropriate.

Categorical (qualitative) variable summaries will include the frequency and percentage of subjects who are in the particular category or each possible value. In general, the denominator for the percentage calculation will be based upon the total number of subjects in the study population within each treatment group, unless otherwise specified. The denominator for by-visit displays will be the number of subjects in the relevant study population with non-missing data at each visit.

The minimum and maximum will be reported with the same degree of precision (ie, the same number of decimal places) as the observed data. Measures of location (mean and median) will be reported to 1 degree of precision more than the observed data and measures of spread (SD) will be reported to 2 degrees of precision more than the observed data.

Percentages will be presented to 1 decimal place, unless otherwise specified.

Unless otherwise indicated, all statistical tests will be conducted at the 0.05 significance level using 2-tailed tests, and *P*-values will be reported. A *P*-value of ≤ 0.10 but > 0.05 will be considered evidence of a trend. Corresponding 95% CIs will be presented for statistical tests.

4.2. Interim Analysis and Data Monitoring

After all subjects in Cohort 3 have completed their last study visits, the database for all subjects in Cohorts 1-3 will be frozen for purposes of an interim analysis of safety and efficacy data. All statistical outputs planned for the final analysis with the exception of the PK oututs will be

generated for the interim analysis. These outputs will exclude any data from Cohort 4 that exists in the database.

As described in Section 3, the DSMB will review the available unblinded safety and tolerability data after 30 subjects randomized in a cohort have completed 2 weeks of treatment. On the basis of this review, the DSMB will make recommendations to the sponsor about initating the subsequent treatment cohort. All responsibilities of the DSMB and details of data to be reviewed will be detailed in the DSMB charter.

The first review will occur when 30 subjects have completed 2 weeks of treatment in cohort 1.

The second review will occur when 30 subjects have completed 2 weeks of treatment in cohort 2.

The third review will occur when 30 subjects have completed 2 weeks of treatment in cohort 3.

The sponsor may request additional reviews, e.g., should any other findings/issues pertaining to safety or efficacy emerge requiring DSMB review. Details of the operation of the DSMB will be developed in conjunction with the members of the DSMB before the first meeting and will be modified as required.

The unblinded analysis will be performed by an independent statistician other than the author of this plan or the person responsible for the primary analysis of this study and treatment codes will be revealed to that party only. The DSMB outputs will not be seen by anyone except the DSMB and the unblinded statistician.

5. Analysis Populations

The following analysis populations are planned for this study:

- **Safety Population (SAF):** The safety population will consist of all patients who receive at least 1 application of study medication.
- **Intent-To-Treat Population (ITT):** The ITT population will consist of all subjects who are randomized.
- **Modified Intent-To-Treat Population (mITT):** The mITT population will consist of all subjects who are randomized and complete the study treatment (subjects who complete 12 weeks of treatment and subjects who complete the treatment period earlier than 12 weeks, due to clearance of all molluscum).
- **Exposure Population:** The exposure population will consist of all subjects who receive at least 1 application of SB206 and had a blood sample collected and analyzed for the hMAP3 plasma concentration.
- **Per-Protocol Population (PP)**: The PP population will consist of all subjects in the mITT population who have no significant protocol deviations that impact the analyses of the efficacy endpoints.

6. General Issues for Statistical Analysis

Table and figure outputs based on the safety population and all listings will be presented by actual treatment received. Table and figure outputs based on the ITT, mITT, or PP populations

will be presented by randomized treatment. Unless otherwise stated, table outputs will contain a pooled vehicle gel column, a column for each SB206 treatment, and a pooled SB206 column.

6.1. Statistical Definitions and Algorithms

6.1.1. Baseline

The last observation recorded prior to the first application of study drug will be used as the baseline observation for all calculations of change from baseline. The time of assessment will not be collected for the assessments on this study with the exeption of the local tolerability assessment at baseline. For assessments without time, the records collected at the Baseline Day 1 visit in the database will be used as baseline. If the Baseline Day 1 assessment is missing, then the assessment collected at screening will be used unless there is an unscheduled assessment after screening and on or before the date of the first application of study drug. If this occurs, the unscheduled assessment will be treated as baseline. For the local tolerability assessment, baseline will be derived using the dates and times of each assessment and the date and time of first application.

6.1.2. Adjustments for Covariates

The primary analysis will include the baseline stratificiation variables of number of lesions (3 to 18; 19 to 70) and atopic dermatitis history (yes/no) as covariates.

6.1.3. Multiple Comparisons

No adjustments will be made for multiple comparisons for this study.

6.1.4. Handling of Dropouts or Missing Data

For the efficacy analyses, missing data will be imputed for dichotomous outcomes (e.g., clearance of all MC) and the continuous outcomes (e.g., lesion counts) using the methods in Section 8, Efficacy Analysis.

6.1.5. Analysis Visit Windows

In order to summarize data collected over time (including unscheduled visits), the following visit windows will be utilized. If multiple assessments fall within a window, the assessment closest to the target day will be used. If two assessments are equidistant from the target day, the earliest assessment will be used. If a scheduled and unscheduled assessment falls on the same day, the scheduled assessment will be used.

Analysis Visit	Target Day	Time Window
Baseline	1	Day -21 to 1
Week 1	8	Day 2 to 11
Week 2	15	Day 12 to 22
Week 4	29	Day 23 to 43
Week 8	57	Day 44 to 71
Week 12	85	Day 72 or later

6.1.6. Pooling of Sites

Not applicable.

6.1.7. Derived Variables

- Time to complete clearance of all MC (days) = date of first complete clearance of all MC – date of first application + 1. Subjects who do not achieve complete clearance prior to their last visit will be censored at their last visit date.
- Time to sustained complete clearance of all MC = date of first complete clearance of all MC where subject maintains complete clearance through Week 12 – date of first application + 1. Subjects who do not achieve sustained complete clearance prior to their last visit will be censored at their last visit date.
- Change from baseline = value at current time point – value at baseline.
- Percent change from baseline = 100*change from baseline/value at baseline.
- Treatment Emergent Adverse Event (TEAE) = any AE with an onset date after the first application of study drug.

6.1.8. Data Adjustments/Handling/Conventions

All collected data will be presented in listings. Data not subject to analysis according to this plan will not appear in any tables or graphs but will be included only in the data listings.

All *P*-values will be displayed in three decimals and rounded using standard scientific notation (e.g., 0.XXX). If a *P*-value less than 0.001 occurs it will be shown in tables as <0.001. If a *P*-value greater than 0.999 occurs it will be shown in tables as >0.999.

Adverse events and medical history will be coded using the MedDRA version 20.1 thesaurus.

Concomitant medications will be coded using World Health Organization Drug Dictionary Enhanced (WHO-DDE) (September 2017).

A treatment related AE is any AE with a relationship to the study drug of definite, probable, or possible.

Missing AE dates will not be imputed. The AE CRF does not allow the study investigators to report partial start and end dates, so partial AE date imputation is not required.

If it is necessary to calculate a subject's age from the (partial or complete) date of birth and the date of Baseline, the floor function will be used to ensure the subject has an integer age.

If partial medication dates occur, the convention for replacing missing dates for the purposes of calculating derived variables is as follows:

For partial medication start dates:

- If the year is unknown, then do not impute the date but assign a missing value.
- If the year is known, but the month or month and day is unknown, then:
    - If the year matches the year of first application date and the end date (if present) is after first application date, or medication is ongoing, then impute as the month and day of the first application date. If this produces a date after the medication end date, assign 01 January.
    - Otherwise, assign 01 January.
- If the year and month are known, but the day is unknown, then:
    - If the month and year match the month and year of the first application date, then impute as the day of the first application date. If this produces a date after the medication end date, assign 01.
    - Otherwise, assign 01.

For partial medication end dates:

- If the year is unknown, then do not impute the date but assign as missing value.
- If the year is known but the month or month and day is unknown, then:
    - If the year matches the year of the last date of the study (date of last contact if subject lost to follow-up; date of completion or early termination otherwise), then impute as the month and day of the last date of the study.
    - Otherwise, assign 31 December.

- If the the year and month are known, but day is unknown, then:
    - If the month and year match the month and year of the last date of the study, then impute as the day of the last date of the study.
    - Otherwise, assign the last day of the month.

In general, for quantitative laboratory values reported as '<X' or '≤X', the lower limit of quantitation (LLOQ) will be used for analysis (ie, the value of X will be used in the analysis for lab values reported as '<X' or '≤X'). Similarly, for quantitative laboratory values reported as '>X' or '≥X', the upper limit of quantitation (ULOQ) will be used for analysis (ie, the value of X will be used in the analysis for lab values reported as '>X' or '≥X').

For analysis purposes, repeat laboratory test results will not be used unless the original laboratory value is missing or indicated as invalid, in which case the first non-missing repeated laboratory value will be used for data analysis.

Screen failure data will not be captured in the database.

7. Study Patients/Subjects and Demographics

7.1. Disposition of Patients/Subjects and Withdrawals

The number of subjects randomized and treated will be summarized by treatment group. The number and percentage of subjects who prematurely discontinued treatment, who completed the study, and who prematurely discontinued the study will be summarized by treatment group. The reasons for treatment and study discontinuation will also be summarized. The number and percentage of subjects in the safety, ITT, mITT, Exposure, and PP populations will be summarized by treatment group.

All disposition information will be listed.

7.2. Protocol Deviations

Protocol deviations will be listed.

7.3. Demographics and Other Baseline Characteristics

Demographic variables such as age, gender, ethnicity, and race, and baseline characteristics such as height, weight, body mass index (BMI), lesion count, and atopic dermatitis history will be summarized by treatment group for the safety, ITT, and mITT populations.

Categorical variables, such as gender, ethnicity, race, and atopic dermatitis history will be summarized using frequencies and percentages. Continuous variables such as age, height, weight, and BMI will be summarized using mean, standard deviation (SD), median, minimum, and maximum. A continuous summary of lesion counts will be presented along with a categorical summary of subjects with 3 to 18 or 19 to 70 lesions at baseline.

Medical history will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) coding system (version 20.1). Medical history information will be listed only.

Demographic information will be listed.

7.4. Exposure and Compliance

For all of the below formulas, *i* = individual subject for the entire treatment period.

- Total days of exposure will be calculated as:

$$\sum_i Days\ on\ Study\ Drug$$

- Study drug compliance will be calculated as:

$$\frac{\sum_i Actual\ Applications\ Applied}{\sum_i Planned\ Applications} \times 100$$

Planned applications is the number planned up to the point of discontinuation. Actual applications applied is planned applications minus the number of applications missed. Total days of exposure and compliance will be summarized by treatment group.

Study drug application and compliance information will be listed. All study drug noncompliance such as missing applications and interruptions in the schedule of administration will be listed in the protocol deviations listing.

8. Efficacy Analysis

8.1. Primary Efficacy Analysis

The primary efficacy variable for this study is the proportion of subjects achieving complete clearance of all MC at Week 12 (subjects who achieve complete clearance before Week 12 need to maintain complete clearance at Week 12) for the mITT population.

Subjects will have their lesion counts measured at Screening, Baseline, Week 1, Week 2, Week 4, Week 8, and Week 12/ET visits. These and any unscheduled visits will be mapped to Baseline, Week 1, Week 2, Week 4, Week 8, and Week 12 analysis visits using the visit windowing algorithm described in section 6.1.5. Complete clearance of all MC at Week 12 is defined as having a lesion count of 0 at Week 12. The number and percentage of subjects with complete clearance at Week 12 will be summarized by treatment group.

The primary efficacy variable will be analyzed using a logistic regression model with treatment, number of lesions at baseline (3-18; 19-70), and atopic dermatitis history (with AD history; without AD history) as factors. The odds ratios between active treatments and vehicle gel, 95% CIs for the odds ratios, and *P*-values for the differences in treatment will be presented. The difference in proportions between active treatments and vehicle gel, 95% CIs for the differences, and *P*-values for the differences in treatment will be presented. The primary analysis will compare each SB206 dose level and pooled SB206 with vehicle gel using the mITT population. Subjects who discontinue the study before the Week 12 analysis visit (study day 71 or earlier) for any reason will be considered not to have achieved complete clearance at Week 12, even if the

subject discontinues after a lesion count of 0. In the event of quasi or complete separation, the logistic regression model will use Firth's penalized maximum likelihood estimation.

The potential for heterogeneity of treatment effects will be assessed by testing treatment-by-stratum interactions: the logistic regression model for the primary analyses will be expanded to include the treatment-by-number of baseline lesions interaction and, separately, the treatment-by-AD history interaction. Any evidence of interactions with treatment (e.g., interaction *P*-value ≤0.10) will be explored further.

A sensitivity analysis of the primary analysis will be conducted by repeating the above analysis using the following analysis populations: ITT; PP; and the mITT population after excluding subjects that have at least one other subject from the same household enrolled in the study.

8.2. Secondary Efficacy Analysis

The secondary efficacy variables for this study include:

- Proportion of subjects achieving complete clearance of all MC at each visit
- Time to complete clearance of all MC
- Proportion of subjects achieving at least 75% reduction from baseline in number of MC at each visit
- Mean change from baseline in number of MC at each visit
- Mean percent change from baseline in number of MC at each visit

The proportion of subjects achieving complete clearance of all MC at each visit will be analyzed using the same logistic regression analysis described in Section 8.1 for each of the other visits in the study. Complete clearance at visits other than Week 12 is defined as having a lesion count of 0 on a visit. Subjects with missing lesion counts at a visit for any reason will be counted as not clear for that visit.

Time to first complete clearance of all MC will be analyzed using Kaplan-Meier methods. The number of subjects, number and percentage of censored subjects, and Kaplan-Meier estimates of first quartile, median, and third quartile as well as the minimum and maximum will be summarized by treatment group. Differences in Kaplan-Meier curves between vehicle gel and both the SB206 dose levels and pooled SB206 group will be tested for significance using the log-rank test. Additionally, Kaplan-Meier curves will be presented by treatment group for the mITT population. Time to first complete clearance is calculated as date of first complete clearance – first application date + 1. If a subject does not achieve complete clearance while on the study, that subject will be censored using the last date on study.

Time to first sustained complete clearance of all MC will be analyzed using the same Kaplan-Meier methods used to analyze time to first complete clearance. Time to first sustained clearance is calculated as date of first complete clearance (where subject maintains clearance through Week 12) – first application date + 1. If a subject does not achieve complete clearance while on the study, that subject will be censored using the last date on study.

Proportion of subjects achieving at least 75% reduction from baseline in number of MC will be

analyzed using the same logistic regression analysis as used to analyze the proportion of subjects achieving complete clearance of all MC at each visit.

Mean change and percent change from baseline in number of MC at each visit will be analyzed using a mixed-model repeated measures (MMRM) analysis with treatment as the main effect, visit, number of lesions at baseline (3-18; 19-70), and atopic dermatitis history (with AD history vs without AD history) as factors and treatment by visit as an interaction term. All post-baseline analysis visits will be included in the model (Week 1, Week 2, Week 4, Week 8, and Week 12). An unstructured covariance matrix will be used to model the within-subject errors. The Kenward-Roger approximation will be used to estimate degrees of freedom.

The least squares (LS) mean change from baseline and percent change from baseline will be presented along with the associated 95% CI within each SB206 treatment, pooled SB206, and vehicle gel group. In comparing treatments (SB206 minus vehicle gel), LS mean differences in change from baseline will be presented along with associated 95% CIs and pairwise treatment *P*-values.

In case of convergence issues, other covariance structures will be used including (but not limited to) autoregressive (AR(1)), compound symmetry (CS), and variance components (VC) with each model fit to find the covariance structure with the best fit. The fit statistics will be compared for all covariance structures; the structure with the smallest Akaike information criterion will be retained as the preferred model.

Two separate MMRM models will be run, the first comparing the individual SB206 treatments with vehicle gel, and the second comparing the pooled SB206 treatment group with vehicle gel.

Mean change and mean percent change from baseline in number of MC at each visit will be plotted over time by SB206 treatment, pooled SB206, and vehicle gel.

All secondary efficacy analyses will be conducted on the mITT and ITT population.

8.3. Exploratory Efficacy Analysis

The exploratory efficacy variables for this study include:

- Proportion of subjects whose lesion count decreases and increases from baseline at each visit
- Absolute number of subjects who show new lesions after once achieving a lesion count of 0 at each visit

The frequency and percentage of subjects at each visit who had an increase, decrease, and no change in lesion count from baseline will be summarized by treatment group.

The frequency and percentage of subjects at each visit and overall who show new lesions after once achieving a lesion count of zero, subjects with a lesion count of 0, and subjects with a lesion count of 0 at a prior visit will be summarized by treatment group.

The exploratory efficacy analyses will be conducted on the mITT population.

9. Safety and Tolerability Analysis

Safety assessments will be performed at scheduled timepoints throughout the study and include physical examination, vital signs, standard clinical laboratory testing (hematology, serum chemistry), methemoglobin measurement, pregnancy test, tolerability evaluation, CMs, and AEs.

All safety analyses will be performed on the Safety population by actual treatment received.

9.1. Adverse Events

Adverse events will be coded using the MedDRA coding thesaurus (version 20.1). Treatment-emergent AEs (TEAEs) will be summarized in all tables. A TEAE is defined as an AE with onset on or after the date of the first application of study drug. Medical histories noted prior to the first study drug administration that worsen after baseline will also be reported as TEAEs and included in the summaries. All AE summary tables will include the number and percentage of subjects as well as the total number of AEs within a category, system organ class (SOC), or preferred term (PT).

An overall summary of the number and percentage of subjects with TEAEs will be provided by treatment group. Frequencies and percentages of the following will be included: subjects with any TEAE, subjects with a related TEAE, subjects with any TEAE leading to discontinuation, subjects with any TEAE leading to death, and subjects with any serious treatment-emergent AE (SAE).

The incidence of TEAEs will be summarized with frequencies and percentages by the following:

- SOC and PT
- SOC, PT, and maximum severity
- SOC, PT, and relationship to study drug
- SAEs by SOC, PT, and maximum severity
- SAEs by SOC, PT, and relationship to study drug

Incidences will be presented alphabetically by SOC and PT. TEAEs with a missing severity will be considered severe and TEAEs with a missing relationship will be considered related.

All adverse events will be presented in a listing.

9.1.1. Adverse Events Leading to Withdrawal

A data listing of AEs leading to withdrawal of study drug will also be provided, displaying details of the event(s) captured on the CRF.

9.1.2. Deaths

Any deaths that occur during the study will be listed.

9.2. Clinical Laboratory Evaluations

Screening and safety chemistry and hematology tests will be performed at Baseline and Week 12 (for subjects who completed the study before Amendment 2) or at the visit corresponding to the last treatment application (for subjects who had not yet completed the study at the time of Amendment 2). All laboratory values will be mapped to the closest study visit, as defined in 6.1.5. Methemoglobin measurements will be collected at Baseline, Week 1, Week 2, Week 4, Week 8, and Week 12. All summaries of laboratory units will be presented using the International System of Units (SI). Observed values and change from baseline at each visit will be summarized by treatment group. Shifts from Baseline to Week 1, Week 2, Week 4, Week 8, and Week 12 for chemistry and hematology results will also be summarized by treatment group. Clinically significant abnormal findings will be reported as AEs.

Chemistry, hematology, and methemoglobin results will be listed by subject and timing of collection. Values falling outside the normal range for chemistry and hematology will be flagged in the listing.

Pregnancy test results will be listed.

9.3. Vital Signs

Descriptive summaries of observed values and changes from baseline will be calculated for systolic blood pressure (mmHg), diastolic blood pressure (mmHg), and heart rate. Vital signs results will be collected at Baseline, Week 1, Week 2, Week 4, Week 8, and Week 12. Vital signs results will be listed.

9.4. Physical Examination

Physical examination results will be listed only.

9.5. Local Tolerability Assessments

Subjects will be assessed at 30 minutes post-application on Baseline and at Week 1, Week 2, Week 4, Week 8, and Week 12 for local tolerability. The investigator will assess the presence and overall degree of irritation (dryness, erythema, and peeling) at the application sites and the score will reflect what the investigator sees at the time of the assessment. The score will represent an "average" across all application sites. Scores of 3 or 4 will be reported as an AE.

Investigator Assessment of Dryness, Erythema, and Peeling

Score	Severity	Description
0	No irritation	No evidence of local irritation/intolerance

1	Mild	Minimal erythema and/or edema, slight glazed appearance
2	Moderate	Definite erythema and/or edema with peeling and/or cracking but does not require treatment modification
3	Severe (report as an AE)	Erythema, edema glazing with fissures, few vesicles or papules
4	Very severe (report as an AE)	Strong reaction spreading beyond the treated area, bullous reaction, erosions

At the Baseline visit, 30 minutes post-application, the subject will be asked to rate the overall severity of their itching and burning/stinging. The assessment will apply only to the time since application of study drug. At Week 1, Week 2, Week 4, Week 8, and Week 12, the subject will be asked to rate the overall severity of their itching and burning/stinging at the treatment areas since their previous visit. Scores of 4 will be reported as an AE.

Subject Assessment of Burning/Stinging and Itching

Score	Severity	Description
0	None	Normal, no discomfort
1	Slight	An awareness, but no discomfort and no intervention required
2	Mild	A noticeable discomfort that causes intermittent awareness
3	Moderate	A noticeable discomfort that causes intermittent awareness and interferes occasionally with normal daily activities
4	Strong/Severe	A definite continuous discomfort that interferes with normal daily activities

The frequencies and percentages of investigator and subject tolerability assessments at each visit will be summarized by treatment group. The vehicle gel treatment group will be split into once daily (QD), twice daily (BID), and overall groups for this analysis. The frequencies and percentages of investigator and subject tolerability assessments at each visit and in relation to baseline will be tabulated in a shift table by treatment group. Tolerability assessment results will be listed.

9.6. Concomitant Medications

Concomitant medications will be coded using World Health Organization Drug Dictionary Enhanced (WHO-DDE) (Version September 01, 2017 or later) thesaurus.

Frequencies and percentages of medications used in the study will be summarized as follows:

- Concomitant medication: a medication with a start date on or after the date of first application of study drug (even if end date is missing) and on or before the last application of study drug, or medications with a start date before the first application of study drug that are ongoing or with a stop date on or after the first application of study drug, will be considered concomitant. If medication dates are incomplete and it is not clear whether the medication was concomitant, it will be assumed to be concomitant.

Details of CMs will be listed by subject, start date, and verbatim term. All medications will be summarized by Anatomic Therapeutic Chemical (ATC) class Level 3 and PT. Furthermore, CMs will be summarized by treatment group. Subjects will be counted once for each ATC and PT.

10. Changes from Planned Analysis

Not applicable.

11. Other Planned Analysis

11.1. Pharmacokinetic Analysis

Plasma concentrations of hMAP3 collected in Cohorts 3 and 4 will be listed. Analysis will be limited to subjects receiving active (SB206) treatment. If quantifiable concentrations are observed, the results will be summarized at Week 12 or at the end of treatment for subjects with complete clearance prior to Week 12 using descriptive statistics including number (n), mean, standard deviation, median, maximum, minimum, % coefficient of variation (CV), and geometric mean. All values below the limit of quantification (BLQ) will be set to 0 for the summary statistics.

12. References

1. US Federal Register. (1998) International Conference on Harmonization; Guidance on Statistical Principles for Clinical Trials. Department of Health and Human Services: Food and Drug Administration [Docket No. 97D-0174]. Federal Register Volume 63, Number 179, pages 49583-49598. September 16, 1998.
2. ASA. (2016) Ethical Guidelines for Statistical Practice. Prepared by the Committee on Professional Ethics, April 2016. http://www.amstat.org/about/ethicalguidelines.cfm
3. The Royal Statistical Society: Code of Conduct, 2014. http://www.rss.org.uk/Images/PDF/join-us/RSS-Code-of-Conduct-2014.pdf.

13. Tables, Listings, and Figures

This section presents the shells for the planned Tables, Listings, and Figures (TLFs) to be programmed. This section provides guidance on the programming specifications (shells) for the planned outputs. After the programming begins, it may be necessary to modify table titles or footnotes or the ordering of rows or columns. Minor, cosmetic changes such as these will not require a modification to the final SAP.

The following reporting conventions will be adopted for the presentation of study data. These conventions will enhance the review process and help to standardize the presentation with common notations.

General Reporting Conventions

- All tables and data listings will be developed in landscape orientation.
- Header and footer rows for tables will repeat on all pages of the table.
- Specialized text styles, such as bolding, italics, borders, shading, and superscripted and subscripted text will not be used in tables, figures, and data listings unless they add significant value to the table, figure, or data listing.
- Only standard keyboard characters should be used in tables and data listings. Special characters, such as nonprintable control characters, printer-specific characters, or font specific characters, will not be used on a table, figure, or data listing.
- A blank row will be included between subjects in the listings.
- In the listings, if text will be repeated on multiple rows for a subject, it will only be displayed in the first row. If the repeated rows cover multiple pages, the text will also be displayed in the first row of each new page.
- Data collected from subjects that did not receive study drug will be listed only.
- Programming notes may be inserted into the shells, these notes will not appear in the final output.

Population Summary Conventions

- Population sizes may be presented for each classification factor as totals in the column header as (N=xxxx), where appropriate.
- All population summaries for categorical variables will include all categories that were planned and for which the subjects may have had a response. Percentages corresponding to null categories (cells) will be suppressed; however, counts and percentages of missing values may be needed.
- All population summaries for continuous variables will include: N, mean, SD, median, minimum, and maximum. Other summaries (e.g., number missing, geometric mean, median, quartiles, 95% CIs, and coefficient of variation [CV] or % CV) may be used as appropriate. The precision of the maximum and minimum will match the maximum precision in the data. The mean and median will have one additional decimal place. The SD will have two additional decimal places.
- All percentages are rounded and reported to a single decimal point (xx.x %)

13.1. Planned Table Descriptions

The following are planned summary tables for protocol number NI-MC201. The table numbers and page numbers are place holders only and will be determined when the tables are produced.

Table 2: Planned Demographic Data Summary Tables

Table Number	Table Title/Summary
13.1 Demographic Data Summary Tables and Figures	
Table 14.1.1	Subject Disposition, All Subjects
Table 14.1.2.1	Demographics and Baseline Characteristics, Safety Population
Table 14.1.2.2	Demographics and Baseline Characteristics, mITT Population
Table 14.1.2.3	Demographics and Baseline Characteristics, ITT Population
Table 14.1.3	Study Drug Exposure and Compliance, Safety Population

13.2. Efficacy Data

Table 3: Planned Efficacy Tables

Table Number	Table Title / Summary
Table 14.2.1.1	Summary of Lesion Counts, mITT Population
Table 14.2.1.2	Summary of Lesion Count Responders, mITT Population
Table 14.2.1.3	Complete Clearance Lesion Count Response by Study Visit and Treatment Group, Logistic Regression, mITT Population
Table 14.2.1.4	Proportion of Subjects with at least a 75% Reduction in Lesion Count from Baseline Response by Study Visit and Treatment Group, Logistic Regression, mITT Population
Table 14.2.1.5	Change from Baseline in Lesion count by Study Visit, MMRM, mITT Population
Table 14.2.1.6	Percent Change from Baseline in Lesion Count by Study Visit and Treatment, MMRM, mITT Population
Table 14.2.1.7	Kaplan-Meier Estimates of Time to First Complete Clearance (Days) from Start of Dosing, mITT Population
Table 14.2.1.8	Kaplan-Meier Estimates of Time to First Sustained Clearance (Days) from Start of Dosing, mITT Population
Table 14.2.1.9	Summary of Increases and Decreases from Baseline in Lesion Count, mITT Population
Table 14.2.1.10	Summary of Subjects that Develop New Lesions after Achieving a Lesion Count of 0, mITT Population
Table 14.2.2.1	Summary of Lesion Counts, ITT Population
Table 14.2.2.2	Summary of Lesion Count Responders, ITT Population
Table 14.2.2.3	Complete Clearance Lesion Count Response by Study Visit and Treatment Group, Logistic Regression, ITT Population
Table 14.2.2.4	Proportion of Subjects with at least a 75% Reduction in Lesion Count from Baseline Response by Study Visit and Treatment Group, Logistic Regression, ITT Population
Table 14.2.2.5	Change from Baseline in Lesion count by Study Visit, MMRM, ITT Population
Table 14.2.2.6	Percent Change from Baseline in Lesion Count by Study Visit and Treatment, MMRM, ITT Population
Table 14.2.2.7	Kaplan-Meier Estimates of Time to First Complete Clearance (Days) from Start of Dosing, ITT Population
Table 14.2.2.8	Kaplan-Meier Estimates of Time to First Sustained Clearance (Days) from Start of Dosing, ITT Population

Table Number	Table Title / Summary
Table 14.2.2.9	Summary of Increases and Decreases from Baseline in Lesion Count, ITT Population
Table 14.2.2.10	Summary of Subjects that Develop New Lesions after Achieving a Lesion Count of 0, ITT Population
Table 14.2.3.1	Complete Clearance Lesion Count Response by Study Visit and Treatment Group, Logistic Regression, PP Population
Table 14.2.4.1	Complete Clearance Lesion Count Response by Study Visit and Treatment Group, Logistic Regression, Excluding Subjects from Same Household, mITT Population

13.3. Safety Data

Table 4: Planned Safety Tables

Table Number	Table Title / Summary
14.3.1 Displays of Adverse Events	
Table 14.3.1.1	Summary of Treatment Emergent Adverse Events, Safety Population
Table 14.3.1.2	Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term, Safety Population
Table 14.3.1.3	Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Severity, Safety Population
Table 14.3.1.4	Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug, Safety Population
Table 14.3.1.5	Summary of Serious Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Severity, Safety Population
Table 14.3.1.6	Summary of Serious Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug, Safety Population
14.3.2 Summary of Deaths, Other Serious and Significant Adverse Events	
Table 14.3.2.1	Listing of Serious Adverse Events, Safety Population
Table 14.3.2.2	Listing of Adverse Events Leading to Study Drug Discontinuation, Safety Population
Table 14.3.2.3	Listing of Adverse Events Leading to Death, Safety Population

Table Number	Table Title / Summary
14.3.5 Laboratory Data Summary Tables	
Table 14.3.5.1.1	Summary of Serum Chemistry Laboratory Results, Safety Population
Table 14.3.5.1.2	Shift of Serum Chemistry Laboratory Results from Baseline, Safety Population
Table 14.3.5.2.1	Summary of Hematology Laboratory Results, Safety Population
Table 14.3.5.2.2	Shift of Hematology Laboratory Results from Baseline, Safety Population
Table 14.3.5.3	Summary of Methemoglobin Results, Safety Population
14.3.6 Other Safety Data Summary Tables	
Table 14.3.6.1	Summary of Vital Signs Results, Safety Population
Table 14.3.6.2	Summary of Local Tolerability Results, Safety Population
Table 14.3.6.2	Shift of Local Tolerability Results, Safety Population
Table 14.3.6.4	Summary of Concomitant Medications, Safety Population

13.4. Pharmacokinetic Data

Table 5: Planned Pharmacokinetic Tables

Table Number	Table Title / Summary
14.4 Pharmacokinetic Data Summary Tables	
Table 14.4.1	Summary of hMAP3 Plasma Concentrations

13.5. Planned Listing Descriptions

The following are planned data and patient/subject data listings for protocol number NI-MC201.

In general, one listing will be produced per CRF domain. All listings will be sorted by treatment, site, and subject number. All calculated variables will be included in the listings.

In all listings a blank line will be placed between each subject. Within a data listing, if an item appears line after line (e.g., repetition of subject number), then only the first occurrence will be displayed.

In data listings, the information for one subject will be kept on one page if at all possible, rather than splitting a subject's information across pages.

Table 6: Planned Listings

Data Listing Number	Data Listing Title / Summary
16.2 Patient/Subject Data Listings	
16.2.1 Patient/Subject Discontinuations/Completions	
Data Listing 16.2.1.1	Subject Disposition
Data Listing 16.2.1.2	Inclusion and Exclusion Criteria
Data Listing 16.2.1.3	Subject Randomization
16.2.2 Protocol Deviations	
Data Listing 16.2.2	Protocol Deviations
16.2.3 Patients/Subjects Excluded from the Efficacy Analyses	
Data Listing 16.2.3	Analysis Populations
16.2.4 Demographic Data and Other Baseline Characteristics	
Data Listing 16.2.4.1	Demographic and Baseline Information
Data Listing 16.2.4.2	Medical History
16.2.5 Compliance and/or Drug Concentration Data	
Data Listing 16.2.5.1	Study Drug Administration

Data Listing Number	Data Listing Title / Summary
Data Listing 16.2.5.2	Study Drug Accountability
Data Listing 16.2.5.3	Pharmacokinetic Blood Concentrations
16.2.6 Individual Efficacy Response Data	
Data Listing 16.2.6.1	Lesion Counts
Data Listing 16.2.6.2	Lesion Count Derived Efficacy Variables, Time to Complete Clearance and 75% Reduction from Baseline
16.2.7 Adverse Event Listings (by Patient/Subject)	
Data Listing 16.2.7.1	Adverse Events
16.2.8 Clinical Observations and Measurements (by Patient/Subject)	
Data Listing 16.2.8.1.1	Serum Chemistry Laboratory Results
Data Listing 16.2.8.1.2	Hematology Laboratory Results
Data Listing 16.2.8.1.3	Methemoglobin Results
Data Listing 16.2.8.2	Pregnancy Test
Data Listing 16.2.8.3	Vital Signs Results
Data Listing 16.2.8.4	Local Tolerability Assessment
Data Listing 16.2.8.5	Physical Examination
Data Listing 16.2.8.6	Concomitant Medications
Data Listing 16.2.8.7	Photography

13.6. Planned Figure Descriptions

The following are planned summary figures for protocol number NI-MC201. The figure numbers and page numbers are place holders only and will be determined when the figures are produced.

Table 6: Planned Figures

Figure Number	Figure Title / Summary
Figure 14.2.1.1.1	Mean Change from Baseline in Lesion Count over Time by Treatment Group, mITT Population
Figure 14.2.1.1.2	Mean Percent Change from Baseline in Lesion Count over Time by Treatment Group, mITT Population
Figure 14.2.1.7	Kaplan-Meier Plot of Time to First Complete Clearance (Days) from Start of Dosing, mITT Population
Figure 14.2.1.8	Kaplan-Meier Plot of Time to Sustained Complete Clearance (Days) from Start of Dosing, mITT Population
Figure 14.2.2.1.1	Mean Change from Baseline in Lesion Count over Time by Treatment Group, ITT Population
Figure 14.2.2.1.2	Mean Percent Change from Baseline in Lesion Count over Time by Treatment Group, ITT Population
Figure 14.2.2.7	Kaplan-Meier Plot of Time to First Complete Clearance (Days) from Start of Dosing, ITT Population
Figure 14.2.2.8	Kaplan-Meier Plot of Time to Sustained Complete Clearance (Days) from Start of Dosing, ITT Population

14. Tables, Listings, and Listing Shells

14.1. Standard Layout for all Tables, Listings, and Figures

Figure 1: Standardized Layout

The following standard layout will be applied to all TLFs in support of this study. Note that programming notes may be added if appropriate after each TLF shell. These notes will not appear on the output.

Novan, Inc Protocol: NI-MC201	Page 1 of x <version>
<Table, Listing, Figure> xx.x.x *<Title of Table Listing or Figure>* *<Study Population and if applicable subgroup Description>*	
Body of Table, Listing or Figure	
Note: *<Note: If directly Applicable>*	
[1] Footnote 1 *<if applicable>* [2] Footnote 2 *<if applicable>* [n] Footnote n *<if applicable>* ….\...\xxxx.sas run on DDMMMYYYY at HH:MM on data extracted on DDMMMYY	

14.2. Planned Table and Figure Shells

Novan, Inc. CONFIDENTIAL Page x of y
Protocol NI-MC201 <Version>

Table 14.1.1
Subject Disposition
All Subjects

Status	Vehicle Gel	SB206 4% BID	SB206 X% XXX	SB206 X% XXX	SB206 X% XXX	All SB206	Overall
Safety Population [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
ITT Population [2]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
mITT Population [3]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Exposure Population [4]	0	0	0	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
PP Population [5]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Prematurely Discontinued Treatment	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Reason for Discontinuation:							
Adverse Event	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Withdrawal by Subject	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Physician Decision	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Protocol Violation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Lost to Follow-up	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Pregnancy	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Lack of Efficacy	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Other	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Completed Study	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Prematurely Discontinued Study	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Reason for Discontinuation:							
Withdrawal by Subject/caregiver	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Lost to Follow-up	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Note: Percentages are based on the number of subjects treated. The denominator for percentage corresponds to the number of subjects in the safety population.
[1] The Safety Population consists of all subjects who are administered study drug.
[2] The Intent-To-Treat Population (ITT) consists of all subjects who are randomized.
[3] The Modified Intent-to-Treat Population (mITT) consists of all subjects who are randomized and complete the study treatment.
[4] The Exposure Population consists of all subjects who received any study drug and had a blood sample collected and analyzed for the hMAP3 plasma concentration.
[5] The Per-Protocol Population (PP) consists of all subjects in the mITT population who have no significant protocol deviations that impact the analyses of the efficacy endpoints.
SOURCE: Listings 16.2.1.1, 16.2.1.2, and 16.2.1.3

Table 14.1.2.1
Demographics and Baseline Characteristics
Safety Population

Variable Statistic or Category	Vehicle Gel (N = XX)	SB206 4% BID (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	Overall (N = XX)
Age (years)						
n	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Std Dev	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Gender						
Female	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Male	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Ethnicity						
Hispanic or Latino	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Not Hispanic or Latino	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Race						
American-Indian or Alaska Native	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Asian	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Black or African-American	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Native Hawaiian or Other Pacific Islander	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
White	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Other	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
More than One Race	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Height (cm)						
n	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Std Dev	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

Note: The denominator for percentage corresponds to the N in each column. N is the number of subjects in the safety population. Subjects are summarized by treatment received. Age is calculated from the date of birth to the date of informed consent. Baseline is defined as the last measurement taken on or before the date of first application of study drug.
SOURCE: Listing 16.2.4.1

Table 14.1.2.1
Demographics and Baseline Characteristics
Safety Population

Variable Statistic or Category	Vehicle Gel (N = XX)	SB206 4% BID (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	Overall (N = XX)
Weight (kg)	XX	XX	XX	XX	XX	XX
n	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Mean	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Std Dev	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Min, Max						
BMI (kg/m^2)	XX	XX	XX	XX	XX	XX
n	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Mean	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Std Dev	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Min, Max						
Lesion Counts at Baseline	XX	XX	XX	XX	XX	XX
n	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Mean	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Std Dev	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Min, Max						
Lesion Counts at Baseline						
3 to 18	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
19 to 70	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Atopic Dermatitis History?						
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Note: The denominator for percentage corresponds to the N in each column. N is the number of subjects in the safety population. Subjects are summarized by treatment received. Age is calculated from the date of birth to the date of informed consent. Baseline is defined as the last measurement taken on or before the date of first application of study drug.
SOURCE: Listing 16.2.4.1

Table 14.1.2.2
Demographics and Baseline Characteristics
mITT Population

Table 14.1.2.3
Demographics and Baseline Characteristics
ITT Population

Table 14.1.3
Study Drug Exposure and Compliance
Safety Population

Variable Statistic	Vehicle Gel (N = XX)	SB206 4% BID (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	Overall (N = XX)
Total Exposure (days)						
n	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Std Dev	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Compliance (%) [1]						
n	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Std Dev	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

Note: N is the number of subjects in the safety population. Subjects are summarized by treatment received.
[1] Compliance is defined as the total number of actual applications applied divided by total number of planned applications *100, summed up over the entire treatment period (up to treatment completion or discontinuation).
SOURCE: Listing 16.2.5.1, 16.2.5.2.1, 16.2.5.2.2

Table 14.2.1.1
Summary of Lesion Counts
mITT Population

Study Visit Statistic	Vehicle Gel (N = XX)	SB206 4% BID (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	Overall (N = XX)
Baseline						
n	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Std Dev	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Week 1 Observed						
n	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Std Dev	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Week 1 Change from Baseline						
n	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Std Dev	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Week 1 Percent Change from Baseline						
n	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Std Dev	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

…**Continue for other visits.**

Note: N is the number of subjects in the mITT population. Subjects are summarized by randomized treatment. Baseline is defined as the last measurement taken on or before the date of first application of study drug.
SOURCE: Listing 16.2.6.1

Figure 14.2.1.1.1
Mean Change from Baseline in Lesion Count over Time by Treatment Group
mITT Population

Programming Note: *x-axis will read "Study Visit (Week), y-axis will read "Mean Change from Baseline in Lesion Count". Curves for vehicle gel, individual active SB206 groups, and a pooled SB206 group will be presented. Footnote will read "Note: Subjects are summarized by randomized treatment. SOURCE: Listing 16.2.6.1.*

Figure 14.2.1.1.2
Mean Percent Change from Baseline in Lesion Count over Time by Treatment Group
mITT Population

Programming Note: *x-axis will read "Study Visit (Week), y-axis will read "Mean Percent Change from Baseline in Lesion Count". Curves for vehicle gel, individual active SB206 groups, and a pooled SB206 group will be presented. Footnote will read "Note: Subjects are summarized by randomized treatment. SOURCE: Listing 16.2.6.1.*

Table 14.2.1.2
Summary of Lesion Count Responders
mITT Population

Study Visit Variable Statistic or Category	Vehicle Gel (N = XX)	SB206 4% BID (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	Overall (N = XX)
Week 1						
Complete Clearance [1]						
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
75% Reduction from Baseline [2]						
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 2						
Complete Clearance [1]						
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
75% Reduction from Baseline [2]						
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
…**Continue for Week 4, Week 8, and Week 12.**						

Note: The denominator for percentage corresponds to the number of subjects with a lesion count measurement at each visit. N is the number of subjects in the mITT population. Subjects are summarized by randomized treatment.
[1] Complete clearance is defined as a subject having a lesion count of 0 at a visit.
[2] At least a 75% reduction in lesion counts from the Baseline visit. Baseline is defined as the last measurement taken on or before the date of first application of study drug.
SOURCE: Listing 16.2.6.1, 16.2.6.2

Table 14.2.1.3
Complete Clearance Lesion Count Response by Study Visit and Treatment Group
Summary of Fitted Point Estimates from Logistic Regression
mITT Population

Study Visit Statistic	Vehicle Gel (N = XX)	SB206 4% BID (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	Overall (N = XX)
Week 1						
n [1]	XX	XX	XX	XX	XX	XX
Responders [2]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Odds Ratio (SB206 vs Vehicle Gel)		X.XX	X.XX	X.XX	X.XX	X.XX
95% CI for Odds Ratio		(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
p-value [3]		X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Difference in Proportion (SB206 vs Vehicle Gel)		X.XX	X.XX	X.XX	X.XX	X.XX
95% CI for Proportion Difference		(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
p-value [3]		X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Week 2						
n [1]	XX	XX	XX	XX	XX	XX
Responders [2]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Odds Ratio (SB206 vs Vehicle Gel)		X.XX	X.XX	X.XX	X.XX	X.XX
95% CI for Odds Ratio		(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
p-value [3]		X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Difference in Proportion (SB206 vs Vehicle Gel)		X.XX	X.XX	X.XX	X.XX	X.XX
95% CI for Proportion Difference		(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
p-value [3]		X.XXX	X.XXX	X.XXX	X.XXX	X.XXX

Continue for Week 4, Week 8, and Week 12. If Firth's penalized maximum likelihood is used, add 'Firth's penalized maximum likelihood estimation is used.' to end of 'Note:' footnote.

Abbreviations: OR = Odds ratio.
Note: The denominator for percentage corresponds to the number of subjects with a lesion count measurement at each visit. N is the number of subjects in the mITT population. Subjects are summarized by randomized treatment.
[1] Number of subjects with a lesion count measurement at each visit.
[2] Number of subjects with complete clearance at a visit. Complete clearance is defined as a subject having a lesion count of 0 at a visit.
[3] Estimates for odds ratio, 95% CI for odds ratio, and p-value are from a logistic regression model, with factors for treatment, number of lesions at baseline (3-18; 19-70), and atopic dermatitis history (with AD history; without AD history) as factors. Baseline is defined as the last measurement taken on or before the date of first application of study drug. The odds ratio is the estimate of the odds of having complete clearance for subjects treated with SB206 relative to that for subjects treated with vehicle gel.
SOURCE: Listing 16.2.6.1, 16.2.6.2

Table 14.2.1.4
Proportion of Subjects with at Least a 75% Reduction in Lesion Count from Baseline Response by Study Visit and Treatment Group
Tabulation of Fitted Point Estimates from Logistic Regression
mITT Population

Same shell as 14.2.1.3, update [2] footnote to: [2] Number of subjects with at least a 75% reduction in lesion count from the 'Baseline' visit.

Table 14.2.1.5
Change from Baseline in Lesion Count by Study Visit and Treatment
Adjusted (Least Squares) Means from MMRM
mITT Population

Study Visit Statistic [1]	Vehicle Gel (N = XX)	SB206 4% BID (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	Overall (N = XX)
Week 1						
n	XX	XX	XX	XX	XX	XX
LS Mean Change from Baseline (SE)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
(95% CI for LS Mean)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)
LS Mean Difference in CFB from Vehicle (SE)		XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
(95% CI for Difference in CFB from Vehicle)		(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)
P-value for Difference in CFB from Vehicle [2]		X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Week 2						
n	XX	XX	XX	XX	XX	XX
LS Mean Change from Baseline (SE)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
(95% CI for LS Mean)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)
LS Mean Difference in CFB from Vehicle (SE)		XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
(95% CI for Difference in CFB from Vehicle)		(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)
P-value for Difference in CFB from Vehicle [2]		X.XXX	X.XXX	X.XXX	X.XXX	X.XXX

Continue for Week 4, Week 8, and Week 12

Abbreviations: CFB = Change from baseline.
Note: N is the number of subjects in the mITT population. Subjects are summarized by randomized treatment. Baseline is defined as the last measurement taken on or before the date of first application of study drug.
[1] Estimates for LS means (at Baseline and Study Visit, change from baseline, and difference from vehicle [ie. change from baseline for SB206 minus change from baseline for vehicle gel]), 95% CI for mean diference from vehicle gel, and P-value for difference from vehicle gel are from a mixed model for repeated measures (MMRM) with treatment, study visit, and treatment-by-study visit interaction as fixed effects, and baseline lesions (3-18; 19-70) and atopic dermatitis history (with AD history; without AD history) as covariates. An unstructured covariance matrix was used to model the within subject correlation.
[2] P-value for testing difference (SB206 minus Vehicle Gel) in change from baseline is 0.
SOURCE: Listing 16.2.6.1

Programming Note: *Update covariance structure and footnote as needed per the SAP text.*

Table 14.2.1.6
Percent Change from Baseline in Lesion Count by Study Visit and Treatment
Summary of Fitted Summary Statistics from MMRM
mITT Population

Programming Note: *Same shell as 14.2.1.5, update "change from baseline" text in body of table and footnote to "percent change from baseline" where applicable. Update 'CFB' to '% CFB'.*

Table 14.2.1.7
Kaplan-Meier Estimates of Time to First Complete Clearance (Days) from Start of Dosing
mITT Population

		SB206				
Statistic	Vehicle Gel (N = XX)	4% BID (N = XX)	X% XXX (N = XX)	X% XXX (N = XX)	X% XXX (N = XX)	Overall (N = XX)
n	XX	XX	XX	XX	XX	XX
n Censored (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Q1, Q3	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
P-value [1]		X.XXX	X.XXX	X.XXX	X.XXX	X.XXX

Note: The denominator for percentage corresponds to the number of subjects in the mITT population. N is the number of subjects in the mITT population. Subjects are summarized by randomized treatment. All estimates calculated using Kaplan-Meier product-limit survival curve methodology. Complete clearance is defined as a subject having a lesion count of 0. Time to complete clearance is calculated as complete clearance date – first application date + 1.
[1] P-value from a log-rank test, comparing SB206 to Vehicle Gel.
SOURCE: Listing 16.2.6.1, 16.2.6.2

Figure 14.2.1.7
Kaplan-Meier Plot of Time to Complete Clearance (Days) from Start of Dosing
mITT Population

Programming Note: *x-axis will read "Days from Start of Dosing", y-axis will read "Proportion of Subjects Yet to Achieve Complete Clearance". Curves for vehicle gel, individual active SB206 groups, and a pooled SB206 group will be presented. Footnote will read "Note: Subjects are summarized by randomized treatment. Complete clearance is defined as a subject having a lesion count of 0. Time to complete clearance is calculated as complete clearance date – first application date + 1. SOURCE: Listing 16.2.6.1, 16.2.6.2*

Table 14.2.1.8
Kaplan-Meier Estimates of Time to Sustained Complete Clearance (Days) from Start of Dosing
mITT Population

		SB206				
Statistic	Vehicle Gel (N = XX)	4% BID (N = XX)	X% XXX (N = XX)	X% XXX (N = XX)	X% XXX (N = XX)	Overall (N = XX)
n	XX	XX	XX	XX	XX	XX
n Censored (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Q1, Q3	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
P-value [1]		X.XXX	X.XXX	X.XXX	X.XXX	X.XXX

Note: The denominator for percentage corresponds to the number of subjects in the mITT population. N is the number of subjects in the mITT population. Subjects are summarized by randomized treatment. All estimates calculated using Kaplan-Meier product-limit survival curve methodology. Sustained complete clearance is defined as a subject having a lesion count of 0 and maintaining a count of 0 through Week 12. Time to sustained complete clearance is calculated as sustained complete clearance date – first application date + 1.
[1] P-value from a log-rank test, comparing SB206 to Vehicle Gel.
SOURCE: Listing 16.2.6.1, 16.2.6.2

Figure 14.2.1.8
Kaplan-Meier Plot of Time to Sustained Complete Clearance (Days) from Start of Dosing
mITT Population

Programming Note: *x-axis will read "Days from Start of Dosing", y-axis will read "Proportion of Subjects Yet to Achieve Sustained Complete Clearance". Curves for vehicle gel, individual active SB206 groups, and a pooled SB206 group will be presented. Footnote will read "Note: Subjects are summarized by randomized treatment. Sustained complete clearance is defined as a subject having a lesion count of 0 and maintaining a count of 0 through Week 12. Time to sustained complete clearance is calculated as sustained complete clearance date – first application date + 1. SOURCE: Listing 16.2.6.1, 16.2.6.2*

Table 14.2.1.9
Summary of Increases and Decreases from Baseline in Lesion Count
mITT Population

Study Visit Statistic	Vehicle Gel (N = XX)	SB206 4% BID (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	Overall (N = XX)
Week 1						
Increase from Baseline	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
No Change from Baseline	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Decrease from Baseline	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 2						
Increase from Baseline	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
No Change from Baseline	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Decrease from Baseline	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 4						
Increase from Baseline	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
No Change from Baseline	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Decrease from Baseline	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 8						
Increase from Baseline	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
No Change from Baseline	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Decrease from Baseline	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 12						
Increase from Baseline	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
No Change from Baseline	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Decrease from Baseline	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Note: N is the number of subjects in the mITT population. The denominator for percentage corresponds to the number of subjects in the mITT population. Subjects are summarized by randomized treatment. Baseline is defined as the last measurement taken on or before the date of first application of study drug.
SOURCE: Listing 16.2.6.1

Table 14.2.1.10
Summary of Subjects that Develop New Lesions after Achieving a Lesion Count of 0
mITT Population

Study Visit Statistic	Vehicle Gel (N = XX)	SB206 4% BID (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	Overall (N = XX)
Week 2						
Number of Subjects with a Previous Lesion Count of 0	XX	XX	XX	XX	XX	XX
Lesion Count >0 After Previous Lesion Count of 0	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 4						
Number of Subjects with a Previous Lesion Count of 0	XX	XX	XX	XX	XX	XX
Lesion Count >0 After Previous Lesion Count of 0	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 8						
Number of Subjects with a Previous Lesion Count of 0	XX	XX	XX	XX	XX	XX
Lesion Count >0 After Previous Lesion Count of 0	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 12						
Number of Subjects with a Previous Lesion Count of 0	XX	XX	XX	XX	XX	XX
Lesion Count >0 After Previous Lesion Count of 0	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Note: N is the number of subjects in the mITT population. Subjects are summarized by randomized treatment. The denominator for percentage corresponds to the number of subjects with a lesion count of 0 at the previous visit.
SOURCE: Listing 16.2.6.1

Table 14.2.2.1
Summary of Lesion Counts
ITT Population

Same shell as 14.2.1.1, update footnote to: *"N is the number of subjects in the ITT population."*

Figure 14.2.2.1.1
Mean Change from Baseline in Lesion Count over Time by Treatment Group
ITT Population

Same shell as 14.2.1.1.1

Figure 14.2.2.1.2
Mean Percent Change from Baseline in Lesion Count over Time by Treatment Group
ITT Population

Same shell as 14.2.1.1.2

Table 14.2.2.2
Summary of Lesion Count Responders
mITT Population

Same shell as 14.2.1.2, update footnote to: *"N is the number of subjects in the ITT population."*

Table 14.2.2.3
Complete Clearance Lesion Count Response by Study Visit and Treatment Group
Summary of Fitted Point Estimates from Logistic Regression
ITT Population

Same shell as 14.2.1.3, update footnote to: *"N is the number of subjects in the ITT population."*

Table 14.2.2.4
Proportion of Subjects with at Least a 75% Reduction in Lesion Count from Baseline Response by Study Visit and Treatment Group
Tabulation of Fitted Point Estimates from Logistic Regression
ITT Population

Same shell as 14.2.1.4, update footnote to: *"N is the number of subjects in the ITT population."*

Table 14.2.2.5
Change from Baseline in Lesion Count by Study Visit and Treatment
Adjusted (Least Squares) Means from MMRM
ITT Population

Same shell as 14.2.1.5, update footnote to: *"N is the number of subjects in the ITT population."*

Table 14.2.2.6
Percent Change from Baseline in Lesion Count by Study Visit and Treatment
Summary of Fitted Summary Statistics from MMRM
mITT Population

Same shell as 14.2.1.6, update footnote to: *"N is the number of subjects in the ITT population."*

Table 14.2.2.7
Kaplan-Meier Estimates of Time to First Complete Clearance (Days) from Start of Dosing
ITT Population

Same shell as 14.2.1.7, update footnote to: *"The denominator for percentage corresponds to the number of subjects in the ITT population. N is the number of subjects in the ITT population."*

Figure 14.2.2.7
Kaplan-Meier Plot of Time to Complete Clearance (Days) from Start of Dosing
ITT Population

Same shell as 14.2.1.7

Table 14.2.2.8
Kaplan-Meier Estimates of Time to Sustained Complete Clearance (Days) from Start of Dosing
mITT Population

Same shell as 14.2.1.8, update footnote to: *"The denominator for percentage corresponds to the number of subjects in the ITT population. N is the number of subjects in the ITT population."*

Figure 14.2.2.8
Kaplan-Meier Plot of Time to Sustained Complete Clearance (Days) from Start of Dosing
ITT Population

Same shell as 14.2.1.8

Table 14.2.2.9
Summary of Increases and Decreases from Baseline in Lesion Count
ITT Population

Same shell as 14.2.1.9, update footnote to: *"The denominator for percentage corresponds to the number of subjects in the ITT population. N is the number of subjects in the ITT population."*

Table 14.2.2.10
Summary of Subjects that Develop New Lesions after Achieving a Lesion Count of 0
ITT Population

Same shell as 14.2.1.10, update footnote to: *"N is the number of subjects in the ITT population."*

Table 14.2.3.1
Complete Clearance Lesion Count Response by Study Visit and Treatment Group
Summary of Fitted Point Estimates from Logistic Regression
PP Population

Same shell as 14.2.1.3, update footnote to: *"N is the number of subjects in the PP population."*

Table 14.2.4.1
Complete Clearance Lesion Count Response by Study Visit and Treatment Group
Summary of Fitted Point Estimates from Logistic Regression
Sensitivity Analysis Excluding Subjects from Same Household
mITT Population

Same shell as 14.2.1.3, add the following text to the footnote: *"Subjects with at least one other subject from the same household enrolled in the study were excluded from the analysis."*

Table 14.3.1.1
Summary of Treatment Emergent Adverse Events
Safety Population

Category	Vehicle Gel (N = XX)	SB206 4% BID (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	Overall (N = XX)
Subjects with at least one TEAE	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Subjects with a Related TEAE [1]	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Subjects with an AE leading to Treatment Discontinuation	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Subjects with an AE leading to Death	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Subjects with at least one SAE	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX

Abbreviations: TEAE = Treatment emergent adverse event; SAE = Serious treatment emergent adverse event.
Note: The denominator for percentage corresponds to the N in each column. N is the number of subjects in the safety population. Subjects are summarized by treatment received. Number of subjects experiencing an event, percentage of subjects experiencing an event, and total number of events are summarized. AEs were coded using MedDRA version 20.1. TEAEs are events that occurred or worsened on or after the first application of study drug. AEs with a missing severity were considered severe.
[1] AEs with a relationship of definite, probable, possible, or missing were considered related.
SOURCE: 16.2.7.1

Table 14.3.1.2
Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Vehicle Gel (N = XX)	SB206 4% BID (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	Overall (N = XX)
Subjects with at least one TEAE	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
SOC 1	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
PT 1	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
PT 2	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
PT 3	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
SOC 2	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
PT 4	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
PT 5	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
...						

Abbreviations: TEAE = Treatment emergent adverse event.
Note: The denominator for percentage corresponds to the N in each column. N is the number of subjects in the safety population. Subjects are summarized by treatment received. Number of subjects experiencing an event, percentage of subjects experiencing an event, and total number of events are summarized. AEs were coded using MedDRA version 20.1. TEAEs are events that occurred or worsened on or after the first application of study drug. Subjects are counted once for each system organ class (SOC) and once for each preferred term (PT). AEs are displayed alphabetically by SOC and PT.
SOURCE: Listing 16.2.7.1

Table 14.3.1.3
Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	Vehicle Gel (N = XX)	SB206 4% BID (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	Overall (N = XX)
Subjects with at least one TEAE	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Any Event (Total)	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Mild	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Moderate	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Severe	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
SOC 1	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Any Event (Total)	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Mild	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Moderate	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Severe	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
PT 1	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Mild	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Moderate	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Severe	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
PT 2	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Mild	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Moderate	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Severe	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
...						

Abbreviations: TEAE = Treatment emergent adverse event.
Note: The denominator for percentage corresponds to the N in each column. N is the number of subjects in the safety population. Subjects are summarized by treatment received. Number of subjects experiencing an event, percentage of subjects experiencing an event, and total number of events are summarized. AEs were coded using MedDRA version 20.1. TEAEs are events that occurred or worsened on or after the first application of study drug. Subjects are counted once for each system organ class (SOC) and once for each preferred term (PT). The severity shown is the greatest severity reported for a particular subject (Severe > Moderate > Mild). AEs with a missing severity were counted as severe. AEs are displayed alphabetically by SOC and PT.
SOURCE: Listing 16.2.7.1

Table 14.3.1.4
Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug
Safety Population

System Organ Class Preferred Term Relationship	Vehicle Gel (N = XX)	SB206 4% BID (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	Overall (N = XX)
Subjects with at least one TEAE	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Any Event (Total)	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Not Related	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Related	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
SOC 1	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Any Event (Total)	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Not Related	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Related	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
PT 1	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Not Related	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Related	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
PT 2	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Not Related	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Related	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
PT 3	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Not Related	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
Related	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX	XX (XX.X%) XX
...						

Abbreviations: TEAE = Treatment emergent adverse event.
Note: The denominator for percentage corresponds to the N in each column. N is the number of subjects in the safety population. Subjects are summarized by treatment received. Number of subjects experiencing an event, percentage of subjects experiencing an event, and total number of events are summarized. AEs were coded using MedDRA version 20.1. TEAEs are events that occurred or worsened on or after the first application of study drug. Subjects are counted once for each system organ class (SOC) and once for each preferred term (PT). The relationship shown is the strongest relationship reported for a particular subject (Related > Not Related). AEs with a missing relationship were counted as related. AEs with a relationship of definite, probable, or possible were considered related. AEs with a relationship of unlikely or unrelated were considered not related. AEs are displayed alphabetically by SOC and PT.
SOURCE: Listing 16.2.7.1

Table 14.3.1.5
Summary of Serious Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Severity
Safety Population

Same shell as 14.3.1.3, update text in first row to: *"Subjects with at least one SAE". Add "SAE = Serious Treatment Emergent Adverse Event" to abbreviation footnote.*

Table 14.3.1.6
Summary of Serious Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug
Safety Population

Same shell as 14.3.1.4, update text in first row to: *"Subjects with at least one SAE". Add "SAE = Serious Treatment Emergent Adverse Event" to abbreviation footnote.*

Table 14.3.2.1
Listing of Serious Adverse Events
Safety Population

Actual Treatment Received: SB206 4% BID

Subject ID	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ End Date (Study Day)	Severity/ Relationship	Outcome/ Study Drug Action Taken/ Medical Treatment Received?	Serious?/ Criteria Met
XXXXXXXXX	XXXXXXXXXX/ XXXXXXXXX/ XXXXXXXXXXXXXX	DDMMMYYYY (XX)/ DDMMMYYYY (XX)	XXXXXXX/ XXXXXXXX	XXXXX/ XXXXXXXXXXXXXXXXX/ XXX	XXXXXXXX/ XXXXXXXXXXXX
XXXXXXXXX	XXXXXXXXXX/ XXXXXXXXX/ XXXXXXXXXXXXXX	DDMMMYYYY (XX)/ DDMMMYYYY (XX)	XXXXXXX/ XXXXXXXX	XXXXX/ XXXXXXXXXXXXXXXXX/ XXX	XXXXXXXX/ XXXXXXXXXXXX
...					

Abbreviations: TEAE = Treatment emergent adverse event.
Note: Study day is calculated relative to the date of first application of study drug. AEs were coded using MedDRA version 20.1. TEAEs are events that occurred or worsened on or after the first application of study drug.

Table 14.3.2.2
Listing of Adverse Events Leading to Study Drug Discontinuation
Safety Population

Same shell as 14.3.2.1, only include AEs leading to study drug discontinuation.

Table 14.3.2.3
Listing of Adverse Events Leading to Death
Safety Population

Same shell as 14.3.2.1, only include AEs leading to death.

Table 14.3.5.1.1
Summary of Serum Chemistry Laboratory Results
Safety Population

Analyte			SB206			
Study Visit Statistic	Vehicle Gel (N = XX)	4% BID (N = XX)	X% XXX (N = XX)	X% XXX (N = XX)	X% XXX (N = XX)	Overall (N = XX)
XXXXXXXXXX (units)						
Baseline						
n	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Std Dev	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Week 1 Observed						
n	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Std Dev	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Week 1 Change from Baseline						
n	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Std Dev	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
…**Include all visits and analytes with data.**						

Note: N is the number of subjects in the safety population. Subjects are summarized by treatment received. Baseline is defined as the last measurement taken on or before the date of first application of study drug.
SOURCE: Listing 16.2.8.1.1

Table 14.3.5.1.2
Shift of Serum Chemistry Laboratory Results from Baseline
Safety Population

Analyte	Baseline Value							
Study Visit	Vehicle Gel (N = XX)				SB206 4% BID (N = XX)			
Category	Low	Medium	High	Total	Low	Medium	High	Total
Analyte 1 (units)								
Week 1								
Low	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Medium	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
High	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Total	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX
Week 2								
Low	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Medium	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
High	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Total	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX
Week 4								
Low	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Medium	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
High	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Total	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX

…Continue for other analytes and visit. Once all analytes have been summarized for first two treatments, begin summary for next two treatments on a new page. Repeat until all treatments, including SB206 Overall group have been summarized. Only summarize visits and analytes with non-missing values

Note: The denominator for percentage corresponds to the number of subjects with a non-missing baseline value and a non-missing value at a visit. N is the number of subjects in the safety population. Subjects are summarized by treatment received. Baseline is defined as the last measurement taken on or before the date of first application of study drug.
SOURCE: Listing 16.2.8.1.1

Table 14.3.5.2.1
Summary of Hematology Laboratory Results
Safety Population

Same shell as 14.3.5.1.1. change source listing to 16.2.8.1.2

Table 14.3.5.2.2
Shift of Hematology Laboratory Results from Baseline
Safety Population

Same shell as 14.3.5.1.2, change source listing to 16.2.8.1.2

Table 14.3.5.3
Summary of Methemoglobin Results
Safety Population

Same shell as 14.3.5.1.1, visits will include Baseline, Week 1, Week 2, Week 4, Week 8 , and Week 12. Change source listing to 16.2.8.1.3

Table 14.3.6.1
Summary of Vital Signs Results
Safety Population

Same shell as 14.3.5.1.1, change "Analyte" text in header to "Parameter". Include supine blood pressure (mmHg), diastolic blood pressure (mmHg), and heart rate (beats/min). Visits will include Baseline and Week 12 Change source listing to 16.2.8.3

Table 14.3.6.2
Summary of Local Tolerability Results
Safety Population

Study Visit	Vehicle Gel			SB206				
Parameter Category	BID (N = XX)	QD (N = XX)	Overall (N = XX)	4% BID (N = XX)	X% XXX (N = XX)	X% XXX (N = XX)	X% XXX (N = XX)	Overall (N = XX)
Baseline								
Investigator assessment of dryness, erythema, and peeling								
0 = No irritation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1 = Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2 = Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3 = Severe (AE)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
4 = Very severe (AE)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subject assessment of burning/stinging and itching								
0 = None	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1 = Slight	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2 = Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3 = Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
4 = Strong/Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Continue for Week 1, Week 2, Week 4, Week 8, and Week 12

Note: The denominator for percentage corresponds to the N in each column. N is the number of subjects in the safety population. Subjects are summarized by treatment received. Baseline is defined as the last measurement taken on or before the date of first application of study drug.
SOURCE: Listing 16.2.8.4

Table 14.3.6.3
Shift of Local Tolerability Results
Safety Population

Assessment / Study Visit / Category	Baseline Value – Vehicle Gel BID (N = XX)					
	0 = None	1 = Mild	2 = Moderate	3 = Severe	4 = Very Severe	Total
Investigator						
Week 1						
0 = None	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1 = Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2 = Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3 = Severe (AE)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
4 = Very severe (AE)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Total	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX
Week 2						
0 = None	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1 = Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2 = Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3 = Severe (AE)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
4 = Very severe (AE)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Total	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX

Continue for Week 4, Week 8, and Week 12, repeat for Subject assessment (update category rows to: 0 = None, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Strong/Severe). Once both assessments have been summarized for first treatment, begin summary for next treatment on a new page. Repeat until all treatments, including Vehicle Gel QD, Vehicle Gel Overall, SB206 dose levels, and SB206 Overall group have been summarized. Subject assessment should start on a new page and the header categories should be updated accordingly.

Note: The denominator for percentage corresponds to the N within each treatment. N is the number of subjects in the safety population. Subjects are summarized by treatment received. Baseline is defined as the last measurement taken on or before the date of first application of study drug.
SOURCE: Listing 16.2.8.4

Table 14.3.6.4
Summary of Concomitant Medications
Safety Population

Anatomic Therapeutic Chemical Classification Preferred Term	Vehicle Gel (N = XX)	SB206 4% BID (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	Overall (N = XX)
Subjects with at least one Prior Medication	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
ATC 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 4	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 5	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 6	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
ATC 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 7	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 8	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 9	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
...						

Note: The denominator for percentage corresponds to the number of subjects in the safety population. N is the number of subjects in the safety population. Subjects are summarized by treatment received. Medications coded using WHO-DDE version 01SEP2017. Concomitant medications are all medications with a start date on or after the first application of study drug, or those with a start date before the first application of study drug that were ongoing or with a stop date on or after the first application of study drug. If medication dates are incomplete and it was not clear whether the medication was concomitant, it was assumed to be concomitant. Medications are displayed alphabetically by Anatomic Therapeutic Class (ATC) and then by Preferred Term (PT). Subjects are counted once for each ATC and PT.
SOURCE: Listing 16.2.8.6

Table 14.4.1
Summary of hMAP3 Plasma Concentrations
Exposure Population

Study Visit Statistic	Vehicle Gel (N = XX)	SB206 4% BID (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	SB206 X% XXX (N = XX)	Overall (N = XX)
Week 12						
n	0	0	0	XX	XX	XX
Mean				XX.X	XX.X	XX.X
Geometric Mean				XX.X	XX.X	XX.X
Std Dev				XX.XX	XX.XX	XX.XX
Median				XX.X	XX.X	XX.X
Min, Max				XX, XX	XX, XX	XX, XX
% CV				XX.X	XX.X	XX.X

Note: N is the number of subjects in the exposure population. Subjects are summarized by treatment received.
SOURCE: Listing 16.2.5.3

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Listing 16.2.1.1
Subject Disposition

Randomized Treatment: Cohort 1, Vehicle Gel 4% BID

Subject ID	Date of Study Discontinuation or Completion	Date of Last Application	Reason for Drug Discontinuation	Reason for Study Discontinuation	If Lost to Follow-up: Date of Last Contact	If Lost to Follow-up: Last Visit	Subject Blind: Broken?	Subject Blind: Date	Subject Blind: Reason
XXXXXX	DDMMMYYYY	DDMMMYYYY		Completed			No		
XXXXXX	DDMMMYYYY	DDMMMYYYY	XXXXXXXXXXXXXXXXXXX	Withdrawal by subject/caregiver			Yes	DDMMMYYYY	XXXXXX
XXXXXX	DDMMMYYYY	DDMMMYYYY		Completed			No		
XXXXXX	DDMMMYYYY	DDMMMYYYY		Completed			No		
XXXXXX	DDMMMYYYY	DDMMMYYYY		Completed			No		

Programming Note: *If reason for discontinuation is AE, physician decision, protocol violation, or other, concatenate reason with ": specify text".*

Listing 16.2.1.2
Inclusion and Exclusion Criteria

Randomized Treatment: Cohort 1, Vehicle Gel 4% BID

Subject ID	Date of Screening	All Inclusion Criteria Met?	Inclusion Criteria Not Met	Any Exclusion Criteria Met?	Exclusion Criteria Met
XXXXXX	DDMMMYYYY	Yes		No	
XXXXXX	DDMMMYYYY	Yes		No	
XXXXXX	DDMMMYYYY	Yes		No	
XXXXXX	DDMMMYYYY	Yes		No	
XXXXXX	DDMMMYYYY	Yes		No	

Listing 16.2.1.3
Subject Randomization

Subject ID	Randomization Date	Randomization ID	Cohort	Randomized Treatment	Actual Treatment
XXXXXX	DDMMMYYYY	XXXX	Cohort X	XXXXXXXXXX	XXXXXXXXXXX
XXXXXX	DDMMMYYYY	XXXX	Cohort X	XXXXXXXXXX	XXXXXXXXXXX
XXXXXX	DDMMMYYYY	XXXX	Cohort X	XXXXXXXXXX	XXXXXXXXXXX
XXXXXX	DDMMMYYYY	XXXX	Cohort X	XXXXXXXXXX	XXXXXXXXXXX
XXXXXX	DDMMMYYYY	XXXX	Cohort X	XXXXXXXXXX	XXXXXXXXXXX

Listing 16.2.2
Protocol Deviations

Format TBD once final protocol deviation list is received.

Listing 16.2.3
Analysis Populations

Randomized Treatment: Cohort 1, Vehicle Gel 4% BID

	Analysis Population					
Subject ID	Safety	mITT	ITT	Exposure	PP	Primary Reason for Exclusion
XXXXXX	Yes	Yes	Yes	No	Yes	XXXXXXXXXXXXXX
XXXXXX	Yes	No	Yes	No	Yes	XXXXXXXXXXXXXX
XXXXXX	Yes	Yes	Yes	No	Yes	XXXXXXXXXXXXXX
XXXXXX	Yes	Yes	Yes	No	Yes	XXXXXXXXXXXXXX
XXXXXX	Yes	Yes	Yes	No	No	XXXXXXXXXXXXXXXXXXX

Listing 16.2.4.1
Demographics and Baseline Characteristics

Randomized Treatment: Cohort 1, Vehicle Gel 4% BID

Subject ID	Date of Birth	Date of Informed Consent/ Assent	Age (years)	Gender	Ethnicity	Race	Family Members Randomized	Randomized (IWRS)/Actual AD Group	Start Date of Current Molluscum
XXXXXX	DDMMMYYYY	DDMMMYYYY/ DDMMMYYYY	XX (XXXX)	F	XXXXXXXXXXXXX	XXXXXXXXXXX	No	AD/AD	DDMMMYYYY
XXXXXX	DDMMMYYYY	DDMMMYYYY/ DDMMMYYYY	XX (XXXX)	F	XXXXXXXXXXXXX	XXXXXXXXXXX	No	No AD/AD	DDMMMYYYY
XXXXXX	DDMMMYYYY	DDMMMYYYY/ DDMMMYYYY	XX (XXXX)	F	XXXXXXXXXXXXX	XXXXXXXXXXX	No	AD/AD	DDMMMYYYY
XXXXXX	DDMMMYYYY	DDMMMYYYY/ DDMMMYYYY	XX (XXXX)	F	XXXXXXXXXXXXX	XXXXXXXXXXX	No	No AD/No AD	DDMMMYYYY
XXXXXX	DDMMMYYYY	DDMMMYYYY/ DDMMMYYYY	XX (XXXX)	F	XXXXXXXXXXXXX	XXXXXXXXXXX	XXXXXX	AD/AD	DDMMMYYYY

Abbreviation: AD = Atopic dermatitis
Note: Randomized AD group is the stratification group subjects were assigned to by the site prior to randomization. Actual AD group is whether or not subjects actually have AD history.

Programming Note: *If multiple races are selected, concatenate the values separating with a semi-colon. If "Other" race is selected, concatenate with specify text – "Other: specify text". If no family memebers have been randomized, list "No". If at least one family member has been randomized, list subject numbers.*

Listing 16.2.4.2
Medical History

Randomized Treatment: Cohort 1, Vehicle Gel 4% BID

Subject ID	System Organ Class/ Preferred Term/ Verbatim Term	Start Date/ End Date
XXXXXX	XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXX	DDMMYYYY/ DDMMYYYY
	XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXX	DDMMYYYY/ DDMMYYYY

Note: Medical history was coded using MedDRA version 20.1.

Listing 16.2.5.1
Study Drug Administration

Randomized Treatment: Cohort 1, Vehicle Gel 4% BID

Subject ID	Study Visit	Study Drug Administered?	Date/Time of Administration
XXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY:HH:MM
XXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY:HH:MM
XXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY:HH:MM
XXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY:HH:MM

Listing 16.2.5.2
Study Drug Accountability

Randomized Treatment: Cohort 1, Vehicle Gel 4% BID

Subject ID	Study Visit	Dispensed or Returned?	Drug Dispensed or Returned at Visit?	Dispensation or Return Date	Kit ID Dispensed or Returned	Weight of Blue Tubes Dispensed or Returned (Units)	Weigh of Yellow Tubes Dispensed or Returned (Units)	Number of Doses Missed Since Last Visit
XXXXXX	XXXXXXXXXXXXX	Dispensed	Yes	DDMMYYYY	XXXX	XX (XX)	XX (XX)	XX
	XXXXXXXXXXXXX	Dispensed	Yes	DDMMYYYY	XXXX	XX (XX)	XX (XX)	XX
	XXXXXXXXXXXXX	Returned	Yes	DDMMYYYY	XXXX	XX (XX)	XX (XX)	
	XXXXXXXXXXXXX	Dispensed	Yes	DDMMYYYY	XXXX	XX (XX)	XX (XX)	XX
	XXXXXXXXXXXXX	Returned	Yes	DDMMYYYY	XXXX	XX (XX)	XX (XX)	
	XXXXXXXXXXXXX	Returned	Yes	DDMMYYYY	XXXX	XX (XX)	XX (XX)	XX
XXXXXX	XXXXXXXXXXXXX	Dispensed	Yes	DDMMYYYY	XXXX	XX (XX)	XX (XX)	XX
	XXXXXXXXXXXXX	Dispensed	Yes	DDMMYYYY	XXXX	XX (XX)	XX (XX)	XX
	XXXXXXXXXXXXX	Returned	Yes	DDMMYYYY	XXXX	XX (XX)	XX (XX)	
	XXXXXXXXXXXXX	Dispensed	Yes	DDMMYYYY	XXXX	XX (XX)	XX (XX)	XX
	XXXXXXXXXXXXX	Returned	Yes	DDMMYYYY	XXXX	XX (XX)	XX (XX)	
	XXXXXXXXXXXXX	Returned	Yes	DDMMYYYY	XXXX	XX (XX)	XX (XX)	XX

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Listing 16.2.5.3
Pharmacokinetic Blood Concentration

Randomized Treatment: Cohort 3, SB206 XXXXXX

Subject ID	Study Visit	PK Sample Collected?	Date of Assesment (Study Day)	hMAP3 Concentration (units)
XXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XX.X
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XX.X
XXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XX.X
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XX.X
XXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XX.X
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XX.X
XXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XX.X
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XX.X

Note: Study day is calculated relative to the date of the first application of study drug.

Listing 16.2.6.1
Lesion Counts

Randomized Treatment: Cohort 1, Vehicle Gel 4% BID

Subject ID	Study Visit	Rater Initial	Assessment Performed?	Assessment Date (Study Day)	Total Number of Lesions	Complete Clearance?	% Reduction from Baseline
XXXXXX	XXXXXXXXXXXX		No	DDMMYYYY (XX)			
	XXXXXXXXXXXX*	XX	Yes	DDMMYYYY (XX)	XX		
	XXXXXXXXXXXX	XXX	Yes	DDMMYYYY (XX)	XX	No	10.2%
	XXXXXXXXXXXX	XXX	Yes	DDMMYYYY (XX)	XX	No	XX%
	XXXXXXXXXXXX	XXX	Yes	DDMMYYYY (XX)	XX	No	XX%
	XXXXXXXXXXXX	XXX	Yes	DDMMYYYY (XX)	XX	Yes	XX%
	XXXXXXXXXXXX	XXX	Yes	DDMMYYYY (XX)	XX	Yes	XX%
XXXXXX	XXXXXXXXXXXX		No	DDMMYYYY (XX)			
	XXXXXXXXXXXX	XX	Yes	DDMMYYYY (XX)	XX		
	XXXXXXXXXXXX	XX	Yes	DDMMYYYY (XX)	XX	XX	XX.X%
	XXXXXXXXXXXX	XX	Yes	DDMMYYYY (XX)	XX	XX	XX.X%
	XXXXXXXXXXXX	XX	Yes	DDMMYYYY (XX)	XX	XX	XX.X%
	XXXXXXXXXXXX	XX	Yes	DDMMYYYY (XX)	XX	XX	XX.X%
	XXXXXXXXXXXX	XX	Yes	DDMMYYYY (XX)	XX	XX	XX.X%

Note: Study day is calculated relative to the date of the first application of study drug. Complete clearance is defined as a subject having a lesion count of 0 at a visit. Visits marked with '*' are baseline. Baseline is defined as the last measurement taken on or before the date of first application of study drug.

Listing 16.2.6.2
Lesion Count Derived Efficacy Variables, Time to Complete Clearance and 75% Reduction from Baseline

Randomized Treatment: Cohort 1, Vehicle Gel 4% BID

Subject ID	Date of First Application of Study Drug	Variable	Clearance Achieved?	Date Achieved or Censoring Date	Days After First Application
XXXXXX	DDMMMYYYY	Complete Clearance	No	DDMMMYYYY	XX
		75% Clearance	Yes	DDMMMYYYY	XX
XXXXXX	DDMMMYYYY	Complete Clearance	XXX	DDMMMYYYY	XX
		75% Clearance	XXX	DDMMMYYYY	XX
XXXXXX	DDMMMYYYY	Complete Clearance	XXX	DDMMMYYYY	XX
		75% Clearance	XXX	DDMMMYYYY	XX
XXXXXX	DDMMMYYYY	Complete Clearance	XXX	DDMMMYYYY	XX
		75% Clearance	XXX	DDMMMYYYY	XX

Note; Days after first application is calculated as date of achievement or censoring – date of first application + 1.

Listing 16.2.7.1
Adverse Events

Randomized Treatment: Cohort 1, Vehicle Gel 4% BID

Subject ID	Any Adverse Events Reported?	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ End Date (Study Day) [1]	Severity/ Relationship	Outcome/ Action Taken with Study Treatment	Serious?/ Criteria Met
XXXXXX	Yes	XXXXXXXXXXXXX/ XXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (XX)/ DDMMMYYYY (XX)	XXXXXXXXXX/ XXXXXXXXXXXX	XXXXXXXXX/ XXXXXXXXXXXXXX	XX/ XXXXXXXXXXX
		XXXXXXXXXXXXX/ XXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (XX)/ DDMMMYYYY (XX)	XXXXXXXXXX/ XXXXXXXXXXXX	XXXXXXXXX/ XXXXXXXXXXXXXX	XX/ XXXXXXXXXXX
		XXXXXXXXXXXXX/ XXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (XX)/ DDMMMYYYY (XX)	XXXXXXXXXX/ XXXXXXXXXXXX	XXXXXXXXX/ XXXXXXXXXXXXXX	XX/ XXXXXXXXXXX

Note: Study day is calculated relative to the date of the first application of study drug. AEs were coded using MedDRA version 20.1.

Programming Note: If multiple SAE criteria are met, concatenate each criteria.

Listing 16.2.8.1.1
Serum Chemistry Laboratory Results

Randomized Treatment: Cohort 1, Vehicle Gel 4% BID

Subject ID	Laboratory Test	Study Visit	Sample Collected?	Date of Assesment (Study Day)	Standard Results	Standard Units	Reference Range [1] Low	High	Flag
XXXXXX	XXXXXXXXXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XX	XX	XX	XX	
		XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XX	XX	XX	XX	
	XXXXXXXXXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XX	XX	XX	XX	
		XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XX	XX	XX	XX	L
	XXXXXXXXXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XX	XX	XX	XX	
		XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XX	XX	XX	XX	H
	XXXXXXXXXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XX	XX	XX	XX	
		XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XX	XX	XX	XX	

Abbreviations: H = High; L = Low; A = Abnormal.
Note: Study day is calculated relative to the date of the first application of study drug.
[1] Reference range is used to identify potentially clinically significant laboratory values.

Listing 16.2.8.1.2
Hematology Laboratory Results

Same shell as 16.2.8.1.1

Listing 16.2.8.1.3
Methemoglobin Results

Randomized Treatment: Cohort 1, Vehicle Gel 4% BID

Subject ID	Study Visit	Methemoglobin Collected?	Assessment Date (Study Day)	Methemoglobin Result (g/dL)
XXXXXX	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX
	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX
	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX
	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX
	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX
XXXXXX	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX
	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX
	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX
	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX
	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX

Note: Study day is calculated relative to the date of the first application of study drug.

Listing 16.2.8.2
Pregnancy Test

Randomized Treatment: Cohort 1, Vehicle Gel 4% BID

Subject ID	Study Visit	Pregnancy Test Performed?	Assessment Date (Study Day)	Pregnancy Test Results
XXXXXX	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX
	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX
	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX
	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX
	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX
XXXXXX	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX
	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX
	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX
	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX
	XXXXXXXXXXXX	Yes	DDMMYYYY (XX)	XX

Note: Study day is calculated relative to the date of the first application of study drug.

Listing 16.2.8.3
Vital Signs Results

Randomized Treatment: Cohort 1, Vehicle Gel 4% BID

Subject ID	Study Visit	Vital Signs Collected?	Date of Assesment (Study Day)	Height (units)	Weight (units)	Body Mass Index (kg/m2)	Heart Rate (bpm)	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)
XXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XX (XX)	XX (XX)	XX	XX	XX	XX
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)				XX	XX	XX
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)				XX	XX	XX
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)				XX	XX	XX
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)				XX	XX	XX
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)				XX	XX	XX
XXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XX (XX)	XX (XX)	XX	XX	XX	XX
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)				XX	XX	XX
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)				XX	XX	XX
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)				XX	XX	XX
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)				XX	XX	XX
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)				XX	XX	XX

Note: Study day is calculated relative to the date of the first application of study drug.

Listing 16.2.8.4
Local Tolerability Assessment

Randomized Treatment: Cohort 1, Vehicle Gel 4% BID

Subject ID	Study Visit	Local Tolerability Collected?	Date/Time of Assessment (Study Day)	Investigator Assessment of Dryness, Erythema, and Peeling [1]	Subject Assessment of Burning/Stinging and Itching [2]
XXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY:HH:MM (XX)	0 = No irritation	0 = None
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	1 = Mild	1 = Slight
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	2 = Moderate	2 = Mild
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	3 = Severe	3 = Moderate
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	4 = Very Severe	4 = Strong/Severe
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	X = XXXXXX	X = XXXXXX
XXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY:HH:MM (XX)	X = XXXXXX	X = XXXXXX
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	X = XXXXXX	X = XXXXXX
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	X = XXXXXX	X = XXXXXX
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	X = XXXXXX	X = XXXXXX
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	X = XXXXXX	X = XXXXXX
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	X = XXXXXX	X = XXXXXX

Note: Study day is calculated relative to the date of the first application of study drug.
[1] 0 = No irritation indicates 'No evidence of local irritation/intolerance'; 1 = Mild indicates 'Minimal erythema and/or edema, slight glazed appearance'; 2 = Moderate indicates 'Definite erythema and/or edema with peeling and/or cracking but does not require treatment modification'; 3 = Severe indicates 'Erythema, edema glazing with fissures, few vesicles or papules'; 4 = Very Severe indicates 'Strong reaction spreading beyond the treated area, bullous reaction, erosions'.
[2] 0 = None indicates 'Normal, no discomfort'; 1 = Slight indicates 'An awareness, but no discomfort and no intervention required'; 2 = Mild indicates 'A noticeable discomfort that causes intermittent awareness'; 3 = Moderate indicates 'A noticeable discomfort that causes intermittent awareness and interferes occasionally with normal daily activities'; 4 = Strong/Severe indicates 'A definite continuous discomfort that interferes with normal daily activities'.

Listing 16.2.8.5
Physical Examination

Randomized Treatment: Cohort 1, Vehicle Gel 4% BID

Subject ID	Study Visit	Physical Examination Performed?	Date of Assessment (Study Day)	Body System	Result	Abnormal Findings	Clinically Significant?
XXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XXXXXXXXXXXXXX	NORMAL		
			DDMMMYYYY (XX)	XXXXXXXXXXXXXX	NORMAL		
			DDMMMYYYY (XX)	XXXXXXXXXXXXXX	ABNORMAL	XXXXXXXXXXXXXX	No
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XXXXXXXXXXXXXX	NORMAL		
			DDMMMYYYY (XX)	XXXXXXXXXXXXXX	NORMAL		
			DDMMMYYYY (XX)	XXXXXXXXXXXXXX	NORMAL		
			DDMMMYYYY (XX)	XXXXXXXXXXXXXX	NORMAL		
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)	XXXXXXXXXXXXXX	NORMAL		
			DDMMMYYYY (XX)	XXXXXXXXXXXXXX	NORMAL		
			DDMMMYYYY (XX)	XXXXXXXXXXXXXX	NORMAL		

Note: Study day is calculated relative to the date of the first application of study drug.

Listing 16.2.8.6
Concomitant Medications

Randomized Treatment: Cohort 1, Vehicle Gel 4% BID

Subject ID	Any Medications Reported?	Concomitant? [1]	Anatomic Therapeutic Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ End Date (Study Day) [1]	Dose (unit)	Route/ Frequency	Reason for use/indication
XXXXXX	Yes	Yes	XXXXXXXXXXXXX/ XXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (XX)/ DDMMMYYYY (XX)	XX (XXX)	XXX/ XX	XXXXXX
		Yes	XXXXXXXXXXXXX/ XXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (XX)/ DDMMMYYYY (XX)	XX (XXX)	XXX/ XX	XXXXXX
		Yes	XXXXXXXXXXXXX/ XXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (XX)/ DDMMMYYYY (XX)	XX (XXX)	XXX/ XX	XXXXXX

Note: Study day is calculated relative to the date of the first application of study drug. Medications were coded using WHO-DD version DDMMMYYYY.
[1] Concomitant indicates medication that started during the treatment period or started prior to first application of study drug and continued during the treatment period.

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Listing 16.2.8.7
Photography

Randomized Treatment: Cohort 1, Vehicle Gel 4% BID

Subject ID	Study Visit	Was Photography Collected?	Collection Date
XXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)
XXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)
XXXXXX	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)
	XXXXXXXXXXXXX	Yes	DDMMMYYYY (XX)

Note: Study day is calculated relative to the date of the first application of study drug. Photography is only obtained for select sites and subjects.

Appendix 1: Premier Research Library of Abbreviations

Abbreviation	Definition
AD	atopic dermatitis
AE	adverse event
BID	twice daily
ATC	anatomical therapeutic class
BMI	body mass index
CRF	case report form
CEC	central ethics committee
CS	clinically significant
CSR	clinical study report
DOB	date of birth
DS	document specialist
DSG	drug safety group
DSM	drug supply management (drug distributor)
DSMB	data safety monitoring board
EC	ethics committee
EMA	European medicines agency
ET	early termination
FDA	food and drug administration
IC	informed consent

Abbreviation	Definition
ICH	international council for harmonization
mITT	modified intent-to-treat
ITT	intent-to-treat
LLOQ	lower limit of quantification
MedDRA	medical dictionary for regulatory activities
MC	Molluscum Contagiosum
MMRM	mixed effect model repeat measurement
NCS	non-clinically significant
NF	non-functional
NOVAN	Novan, Inc.
PD	protocol deviation
PE	physical examination
PP	per-protocol
QD	once daily
SAE	serious adverse event
SAP	statistical analysis plan
SAS®	a software system used for data analysis
SBP	systolic blood pressure
SC	study coordinator
SCR	software change request

Abbreviation	Definition
SD	standard deviation
SDS	study design specifications
SDTM	study data tabulation model
SI	International System of Units
SOC	system organ class
SOP	standard operating procedure
TEAE	treatment-emergent adverse event
TIW	three times a week
UPT	urine pregnancy test
WHO	world health organization
WHO-DD	world health organization drug dictionary