STATISTICAL ANALYSIS PLAN

A Multicenter, Vehicle-controlled, Randomized Study to Evaluate the Safety, Tolerability, Systemic Pharmacokinetics, and Pharmacodynamics of AXR-159 Ophthalmic Solution 3 mg/mL, 30 mg/mL, and 50 mg/mL in Patients with Dry Eye Disease (DED)

Sponsor: AxeroVision, Inc.

Protocol Number: AXR201701

Author: Garrick Wallstrom
Principal Research Biostatistician
Statistics & Data Corporation

Date: 25-January-2019

Version: 2.0

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Statistical Analysis Plan Approval

Prepared by: _____ 25 Jan 2019

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Principal Research Biostatistician

Statistics & Data Corporation

Reviewed by: _____ 25 JAN 2019

Kirk Bateman, MS — Date

Senior Director, Biostatistics and SAS Programming

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Charles Bosworth, PhD — Date IN AUSTRALIA

Vice President, Head of Clinical Development

AxeroVision, Inc.

SDC
Statistics & Data Corporation

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Charles Bosworth, PhD Date

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AxeroVision, Inc.

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List of Abbreviations

AE	Adverse Event
ANOVA	Analysis of Variance
ATC	Anatomical Therapeutic Chemical Classification
BCVA	Best-Corrected Visual Acuity
BID	Bis in die (twice daily)
CAE	Controlled Adverse Environment
CI	Confidence Interval
CRF	Case Report Form
CS	Clinically Significant
DED	Dry Eye Disease
eCRF	Electronic Case Report Form
ETDRS	Early Treatment of Diabetic Retinopathy Study
HIPAA	Health Information Portability and Accountability Act
IB	Investigator's Brochure
ICCS	Inferior Corneal Staining Score
ICH	International Conference on Harmonisation
IOP	Intraocular Pressure
IP	Investigational Product
LOCF	Last Observation Carried Forward
logMAR	Logarithm of the Minimum Angle of Resolution
MCMC	Markov Chain Monte Carlo
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified Intent-to-Treat
mITT2	Modified Intent-to-Treat 2
NCS	Not clinically significant
OD	Oculus Dextrus (Right Eye)
OS	Oculus Sinister (Left Eye)
OSDI	Ocular Surface Disease Index
PDF	Portable Document Format
PP	Per Protocol
PT	Preferred Term
RDC	Remote Data Capture
RTF	Rich Text Format
SAAS	Software-as-a-Service
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SANDE	Symptom Assessment in Dry Eye
SD	Standard Deviation
SDC	Statistics and Data Corporation, Incorporated
SOC	System Organ Class

TEAE	Treatment-Emergent Adverse Event
TE-SAE	Treatment-Emergent Serious Adverse Event
TFBUT	Tear Film Break-Up Time
TID	Ter in die (three times daily)
VA	Visual Acuity
VAS	Visual Analog Scale
WHO DDE	World Health Organization Drug Dictionary Enhanced

1. Introduction

The purpose of this statistical analysis plan (SAP) is to describe the planned analyses and reporting for protocol AXR201701, version 1 dated 17Feb2018.

This SAP is being written with due consideration of the recommendations outlined in the most recent International Conference on Harmonization (ICH) E9 Guideline entitled Guidance for Industry: Statistical Principles for Clinical Trials and the most recent ICH E3 Guideline, entitled Guidance for Industry: Structure and Content of Clinical Study Reports.

This SAP describes the data that will be analyzed and the subject characteristics, efficacy, and safety assessments that will be evaluated. This SAP provides details of the specific statistical methods that will be used. The statistical analysis methods presented in this document will supersede the statistical analysis methods described in the clinical protocol. If additional analyses are required to supplement the planned analyses described in this SAP they may be completed and will be identified in the CSR.

2. Study Objectives

The primary objectives for Stage 1 are to evaluate the safety, tolerability, and exploratory pharmacodynamics of up to 2 different concentrations of AXR-159 Ophthalmic Solution (30 mg/mL or 50 mg/mL) dosed three-times daily (TID) or twice-daily (BID) for up to 12 weeks compared to its vehicle in patients with Dry Eye Disease (DED). The primary objectives for Stage 2 are to evaluate the safety, tolerability, and pharmacodynamics of up to 3 different concentrations of AXR-159 Ophthalmic Solution (3 mg/mL, 30 mg/mL or 50 mg/mL) dosed TID or BID for up to 12 weeks compared to its vehicle in patients with DED.

2.1 Primary Variables

Primary efficacy measures for Stage 1 and Stage 2 include changes from baseline to Month 3 in total sodium fluorescein corneal staining (Oxford and Ora Calibra® scales), sodium fluorescein corneal staining in the inferior cornea (Ora scale), patient symptoms of dryness (visual analog scale [VAS]), and total Ocular Surface Disease Index (OSDI).

2.2 Secondary Variables

Secondary efficacy measures for Stage 1 and Stage 2 include Schirmer's test without anesthesia, tear film break-up time (TFBUT), conjunctival redness score, sodium fluorescein corneal staining (Oxford and Ora Calibra® scales), lissamine green conjunctival staining (Oxford and Ora Calibra® scales), ocular discomfort score, Ora Calibra® Ocular Discomfort & 4-Symptom Questionnaire, patient symptoms (VAS), OSDI (total and subscales), Symptom Assessment iN Dry Eye (SANDE), and tear sampling for mechanism of action biomarkers.

2.3 Exploratory Variables

There are no exploratory variables.

2.4 Safety Variables

The safety variables include the following:

- Adverse events (AE) (ocular and non-ocular)
- Ora Calibra® Drop Comfort Assessment
- Best-corrected visual acuity (BCVA)
- Slit-lamp biomicroscopy
- Intraocular pressure (IOP)
- Ophthalmoscopy
- Ora Calibra® Conjunctival Redness for Dry Eye Scale
- Vital signs
- Laboratory tests (chemistry, hematology, urinalysis)
- Urine pregnancy test

2.5 Statistical Hypotheses

The statistical hypotheses are stated in terms of one-sided hypotheses, although statistical testing will be two-sided. All hypotheses are Pre-Controlled Adverse Environment (CAE)®. The null and alternative hypotheses, based on the primary variables, are as follows:

H_{01}: There is no difference between AXR-159 Ophthalmic Solution (50 mg/ml, 30 mg/ml or 3 mg/ml, TID or BID) and vehicle (TID or BID) in the change from baseline to Month 3 in inferior corneal staining score in the study eye.

H_{11}: The change from baseline to Month 3 in inferior corneal staining score in the study eye is less with AXR-159 Ophthalmic Solution (50 mg/ml, 30 mg/ml or 3 mg/ml, TID or BID) than with vehicle (TID or BID).

H_{02}: There is no difference between AXR-159 Ophthalmic Solution (50 mg/ml, 30 mg/ml or 3 mg/ml, TID or BID) and vehicle (TID or BID) in the change from baseline to Month 3 in total corneal staining score in the study eye.

H_{12}: The change from baseline to Month 3 in total corneal staining score in the study eye is less with AXR-159 Ophthalmic Solution (50 mg/ml, 30 mg/ml or 3 mg/ml, TID or BID) than with vehicle (TID or BID).

H_{03}: There is no difference between AXR-159 Ophthalmic Solution (50 mg/ml, 30 mg/ml or 3 mg/ml, TID or BID) and vehicle (TID or BID) in the change from baseline to Month 3 in eye dryness.

H_{13}: The change from baseline to Month 3 in eye dryness is less with AXR-159 Ophthalmic Solution (50 mg/ml, 30 mg/ml or 3 mg/ml, TID or BID) than with vehicle (TID or BID).

H_{04}: There is no difference between AXR-159 Ophthalmic Solution (50 mg/ml, 30 mg/ml or 3 mg/ml, TID or BID) and vehicle (TID or BID) in the change from baseline to Month 3 in total OSDI score.

H_{14}: The change from baseline to Month 3 in total OSDI score is less with AXR-159 Ophthalmic Solution (50 mg/ml, 30 mg/ml or 3 mg/ml, TID or BID) than with vehicle (TID or BID).

In the hypotheses above, dosing (TID or BID) of the vehicle will match the dosing of the active treatment.

3. Study Design and Procedures

3.1 General Study Design

This is a multicenter, double-masked, vehicle-controlled, randomized, parallel group study carried out in 2 stages (Stage 1: AXR-159 Ophthalmic Solution (30 mg/mL or 50 mg/mL) dosed TID or BID; Stage 2: AXR-159 Ophthalmic Solution (3 mg/mL, 30 mg/mL or 50 mg/mL) TID or BID.

Subjects with signs and symptoms of DED will be randomly assigned in a 4:1 (Cohorts 1-3 in Stage 1), 1:1 (Expansion Cohort in Stage 1) or up to a 2:2:2:2:1:1:1 (Stage 2; AXR-159 50 mg/mL TID : AXR-159 50 mg/mL BID : AXR-159 30 mg/mL TID : AXR-159 3 mg/mL TID : Vehicle TID : Vehicle BID : AXR-159 50 mg/ML + Artificial Tear TID or BID) ratio to receive either a single concentration of AXR-159 Ophthalmic Solution or AXR-159 Ophthalmic Solution Vehicle. A screening visit will be followed by a baseline period where subjects will dose with AXR-159 Ophthalmic Solution Vehicle, TID for 14 days. At the end of the baseline period patients who still exhibit signs and symptoms of DED will be enrolled into a 3-month treatment period (See Protocol Appendix 1 for study visit structure across Stages 1 and 2 and Protocol Figure 6.1-1 for the study flow diagram).

Study visits will be referred to in all tables and listings as the expected study day corresponding to the visit to enable reviewers to understand the assessment timing without referring to the protocol visit schedule. The following table shows the scheduled study visits, their planned study day, and the acceptable visit window for each study visit:

Scheduled Visit	Planned Study Day	Visit Window
Visit 1	Day -14	+/- 2 Days
Visit 2	Day 1	N/A
Visit 3	Day 15	+/- 2 Days
Visit 4	Day 43	+/- 2 Days
Visit 5	Day 85 (Month 3)	+/- 2 Days

3.2 Schedule of Visits and Assessments

The schedule of visits and assessments is provided below.

Procedure	Visit 1 Day -14 ± 2		Visit 2 Day 1	Visit 3 Day 15 ± 2	Visit 4 Day 43 ± 2	Visit 5 Day 85 ± 2	
	Pre CAE®	Post CAE®	Non-CAE®	Non-CAE®	Non-CAE®	Pre-CAE®	Post-CAE®
Informed Consent / HIPAA	X						
Medical / Medication History and Demographics	X						
Medical / Medication Update			X	X	X	X	
Vehicle Run-in Collection			X				
Study Drug Collection			X	X	X	X	
Review of Qualification Criteria	X	X	X				
Adverse Event Query		X	X	X	X	X	X
Pregnancy Test	X[a]					X[a]	
Visual Analog Scale	X	X	X	X	X	X	X
Ora Calibra® Ocular Discomfort Scale	X	X	X	X	X	X	X
Ora Calibra® Ocular Discomfort & 4-Symptom Questionnaire	X	X	X	X	X	X	X
SANDE Questionnaire	X		X	X	X	X	
OSDI© Questionnaire	X		X	X	X	X	
Visual Acuity (ETDRS)	X		X	X	X	X	
Vital Signs	X		X			X	
Bulbar Conjunctival Hyperemia	X	X	X	X	X	X	X
Slit-lamp Biomicroscopy	X	X	X	X	X	X	X
Tear Collection (Selected Sites)			X			X	
Oculus Keratograph 5®	X[b]		X[b]	X[b]	X[b]	X[b]	
TFBUT	X	X	X	X	X	X	X
Fluorescein Staining (Ora & Oxford Scales)	X	X	X	X	X	X	X
Lissamine Green Staining (Oxford Scale)	X	X	X	X	X	X	X
15 Minute Wait Period	X		X	X	X	X	
Schirmer's Test	X		X	X	X	X	
CAE® Exposure	X					X	
Discomfort Grading during CAE® Exposure	X					X	
Intraocular Pressure		X	X	X	X		X
Ophthalmoscopy Exam		X[c]					X[c]
CBC and Differential Blood Draw		X					X
Pharmacokinetic Blood Draw		X[d]			X[d]		
Randomization			X				
Vehicle Run-In Dispensation		X					

Procedure	Visit 1 Day -14 ± 2		Visit 2 Day 1	Visit 3 Day 15 ± 2	Visit 4 Day 43 ± 2	Visit 5 Day 85 ± 2	
	Pre CAE®	Post CAE®	Non-CAE®	Non-CAE®	Non-CAE®	Pre-CAE®	Post-CAE®
Vehicle Run-In Instillation		X					
Study Drug Dispensation			X	X	X		
Study Drug Instillation			X	X	X		X
Ora Calibra® Drop Comfort Assessment			X		X		X
Exit Subject from Study							X

[a] To women of child-bearing potential, as defined.
[b] TFBUT and Tear meniscus height only; only at selected sites

[c] Ophthalmoscopy examination will be dilated at randomization and undilated for Visit 5 unless dilation is necessary
[d] Blood samples for pharmacokinetic analysis will only be collected for Stage 1, the first 40 patients in the expansion cohort as follows: Visit 2: pre-dose, Visit 4: pre-dose, 15 min, 30 min, 60 min, 90 min, and 3 hr, & 6 hr post dose.

4. Study Treatments

4.1 Method of Assigning Subjects to Treatment Groups

Prior to initiation of study run-in (at Visit 1), each subject who qualifies for entry will be assigned a screening number. All screening numbers will be assigned in strict numerical sequence at a site and no numbers will be skipped or omitted. If all inclusion and exclusion criteria are met at Visits 1 and 2, each qualifying subject will then be assigned a randomization number at the end of Visit 2.

A randomization schedule will be provided to each investigational site. The randomization schedule will use block randomization stratified by site, such that there will be an approximate equal number of subjects assigned to each of the two treatment arms at each site for the Stage 1, Expansion Cohort. For Stage 1, Cohorts 1-3 patients with signs and symptoms of DED will be randomly assigned in a 4:1 ratio to receive either a single concentration of AXR-159 Ophthalmic Solution or AXR-159 Ophthalmic Solution Vehicle. The site staff will dispense to the patient the study kit labelled with the corresponding randomization number. The randomization number will be recorded on the patient's source document and eCRF. New kits will be dispensed at Visits 2, 3, and 4 based on the subject's randomization. The Sponsor, Investigators, and study staff will be masked during the randomization process and throughout the study.

During the run-in period, the patients will all be supplied with AXR-159 Ophthalmic Solution Vehicle. Patients will be informed that they will receive only vehicle during the 2-week run-in period. Following the run-in period the patient, site personnel, the sponsor and patients will be masked to the treatment

assignment for the 3 month treatment period. All study medication will be provided in identical unit of dose vials and cartons to maintain masking of the study.

For both Stages 1 and 2, patients with signs and symptoms of DED will be randomly assigned in a 4:1 (Stage 1, Cohorts 1-3) ratio, a 1:1 (Stage 1, Expansion Cohort) ratio, or to a 2:2:2:2:1:1:1 (Stage 2) ratio to receive either a single concentration of AXR-159 Ophthalmic Solution or AXR-159 Ophthalmic Solution Vehicle. For the expansion cohort in Stage 1 and Stage 2, subjects will be randomized by strata as follows:

- Site
- Baseline eye dryness score ≥ 60, < 60
- Baseline inferior corneal staining > 1.5, ≤ 1.5

Subjects will not be stratified in Cohorts 1, 2 and 3 in Stage 1.

The Subject ID that will be used to identify subjects in all datasets and listings for this study will be of the form xx-yyy, where xx is a two-digit site number and yyy is a three-digit screening number.

4.2 Masking and Unmasking

An independent biostatistician who is not otherwise involved in the trial will generate the complete randomized study drug kit list. The subject, Sponsor, Investigators and study staff will be masked during the randomization process and throughout the study. All study medication will be provided in identical unit of dose vials and cartons to maintain masking of the study.

When necessary for the safety and proper treatment of the patient, the investigator can unmask the patient's treatment assignment to determine which treatment has been assigned and institute appropriate follow-up care. When possible, the sponsor (AxeroVision Inc.) should be notified prior to unmasking study medication. The investigator should inform the sponsor (AxeroVision Inc.) of the unmasking if there is no notification prior to the unmasking.

A report of the results of this study may be published, sent to the appropriate health authorities in any country in which the study drug may ultimately be marketed, and published in part as required by appropriate health authorities (e.g., Clinical Trials posting and disclosure), but the patient's name will not be disclosed in these documents.

Patients will be informed that the study is posted and the results eventually disclosed by appropriate health authorities (e.g., Clinical Trials posting or freedom of information by the FDA).

5. Sample Size and Power Considerations

The sample size is determined empirically. Xiidra achieved a 0.25 unit difference between lifitegrast ophthalmic solution and vehicle in mean change from baseline to day 84 in inferior corneal staining and

a standard deviation of approximately 0.75 in Phase 2. Sample sizes for this study are based on detecting a 0.35 unit difference between the active and vehicle groups, assuming a standard deviation of 0.75. In Stage 1 the number of expected enrolled subjects varies between 43 and 53 subjects in the active group and between 37 and 47 subjects in the vehicle group. In Stage 2 the number of expected enrolled subjects is 60 in the active group and 30 to 60 subjects in the vehicle group. Thus, the combined sample provides between 103 and 113 subjects in the active group and between 67 and 77 subjects in the matching vehicle group or between 97 and 107 subjects in the combined vehicle group. Under these assumptions and allowing a dropout rate of 10%, sample sizes of 93 in the active treatment group and 60 in the vehicle group will yield 80% power to show a significant difference at the $\alpha = 0.05$ level using a two-sample t-test.

6. Data Preparation

The clinical study database for AXR201701 will be developed and tested in iMedNet™ v1.174.2 or higher. iMedNet™ is delivered as a single-instance multi-tenant Software-as-a-Service (SaaS) EDC system and is developed, maintained, and hosted by MedNet Solutions located in Minnetonka, Minnesota. Therefore, over the duration of the study, MedNet Solutions may apply system updates to the EDC system as part of their continuous improvement efforts. The version of the system at the time of the study completion will be recorded on the Study Lock CheckList.

Data from source documents will be entered into the eCRF by site personnel. After data are entered into the clinical study database, electronic edit checks and data review will be performed. All data validation specifications and procedures are detailed in the Data Validation Manual as a separate document. When the database has been declared to be complete and accurate, the database will be locked. Any changes to the database after data have been locked can only be made with the approval Ora, Inc. and AxeroVision, Inc. in consultation with SDC.

All analyses outlined in this document will be carried out after the following have occurred:

- All data management requirements are met according to SDC standard operating procedures, including data entry, performance of edit and validation checks, documentation and resolution of data queries, and database lock with written authorization provided by appropriate SDC and Sponsor personnel;
- Protocol deviations have been identified and status defined (major/minor deviations);
- Analysis populations have been determined; and
- Randomized treatment codes have been unmasked

7. Analysis Populations

The statistical analysis of safety data will be performed for the safety population. The analysis of baseline and efficacy data will be performed for the modified intent-to-treat (mITT) population. The

primary efficacy analysis will also be performed on the modified intent-to-treat 2 (mITT2) and the per protocol (PP) populations as sensitivity analyses.

7.1 Modified Intent-to-Treat

The mITT population includes all randomized subjects that have baseline and at least 1 post-baseline assessment for 1 or more of the efficacy measurements. Subjects in the mITT population will be analyzed as randomized.

7.2 Modified Intent-to-Treat 2

The mITT2 population includes all subjects in the mITT population that have baseline inferior corneal staining score in the study eye > 1.5. Subjects in the mITT2 population will be analyzed as randomized.

7.3 Per Protocol

The per protocol (PP) population includes subjects in the mITT population who do not have significant protocol deviations and who complete the study. Protocol deviations will be assessed prior to database lock and unmasking. The PP population will be analyzed using observed data only for primary efficacy variables. Subjects in the PP population will be analyzed as treated.

7.4 Safety

The Safety population includes all randomized subjects who have received at least one dose of the investigational product. The Safety population will be analyzed for all safety assessments. Subjects in the Safety population will be analyzed as treated.

8. General Statistical Considerations

8.1 Unit of Analysis

Safety endpoints will be analyzed for both eyes. For efficacy endpoints, the unit of analysis will be the study eye, or the “worst eye,” as defined by the following:

Study Eye/Worst Eye: Eyes are eligible for analysis if they meet all of the inclusion criteria. In the case that both eyes are eligible for analysis, the study eye will be the eye with worse (higher) inferior corneal staining score (Ora Calibra® scale) on Day 1. If the inferior corneal staining score is the same in both eyes, then the right eye will be selected as the study eye.

8.2 Missing or Inconclusive Data Handling

The primary efficacy analyses will be performed using LOCF methodology. For the LOCF analyses of the pre-CAE® primary efficacy variables at Month 3 (Visit 5 [Day 85 ± 2]), the last value from the previous visits will be carried forward. Only pre-CAE® or non-CAE® time points will be used to impute a missing pre-CAE® value.

An analysis using observed data only will also be performed for the primary efficacy variables. As additional sensitivity analyses, Markov Chain Monte Carlo (MCMC) multiple imputation methodology will be used to impute missing data for the analyses of the primary efficacy variables.

No secondary efficacy endpoints or safety endpoints will be imputed.

8.3 Definition of Baseline

Baseline measures are defined as the last measure prior to the initiation of study treatment, usually at Day 1. If a measure is taken both pre-CAE® and post-CAE®, the baseline will be the last time point matched value prior to the initiation of study treatment. For post-CAE® measures, this will be at Day -14. For changes from pre-CAE® to post-CAE® post first treatment, the change from pre-CAE® to post-CAE® at Day -14 will be considered the baseline value.

Changes from baseline will be calculated as visit minus baseline and summarized by treatment and visit as described above. Treatment comparisons between an active treatment and vehicle will be calculated as active minus vehicle.

8.4 Data Analysis Conventions

All data analysis will be performed by Statistics & Data Corporation (SDC) after the study is completed and the database has been locked and released for unmasking. Statistical programming and analyses will be performed using SAS® Version 9.4 or higher. Output will be provided in rich text format (RTF) for tables and portable document format (PDF) for tables, listings, and figures using landscape orientation. All study data will be listed by subject, treatment, and visit (as applicable) based on all randomized subjects unless otherwise specified.

Summaries for continuous and ordinal variables will include the number of observations (n), arithmetic mean, standard deviation (SD), median, minimum, and maximum). Minima and maxima will be reported with the same precision as the raw values; means and medians will be presented to one additional decimal place than reported in the raw values. SDs will be presented to two additional decimal places than reported in the raw values. Summaries for discrete variables will include frequency counts and percentages. All percentages will be rounded to one decimal place (i.e., XX.X%). Differences between active treatment groups and vehicle will be calculated as Active minus Vehicle and change from baseline will be calculated as follow-up visit minus baseline. The baseline measure will be defined as the last non-missing measure prior to initiation of investigational treatment.

Statistical comparisons between each AXR-159 Ophthalmic Solution group will be to the vehicle group at matched dosing frequency (TID or BID). AXR-159 Ophthalmic Solution plus Artificial Tear group will be compared to both AXR-159 Ophthalmic Solution and to the vehicle group at matched dosing frequency.

A final database lock will occur at the completion of Stage 2 and the safety, tolerability, and efficacy data from both Stage 1 and 2 will be analyzed separately and in a combined fashion to fully leverage the advantage of this two-stage study design.

All statistical tests will be two-sided with a significance level of 0.05 ($\alpha = 0.05$) unless otherwise specified. Confidence intervals (CI) for differences between treatment groups will be two-sided at 95% confidence. All p-values will be rounded to four decimal places; p-values less than 0.0001 will be presented as "<0.0001"; p-values greater than 0.9999 will be presented as ">0.9999".

Unless otherwise specified, summaries will be presented by treatment group and, where appropriate, visit.

8.5 Adjustments for Multiplicity

This is a Phase 2 study to evaluate safety, tolerability, systemic pharmacokinetics, and pharmacodynamics. All efficacy analyses will be exploratory. There will be no multiplicity adjustments for the multiple treatment groups or multiple primary endpoints.

9. Disposition of Subjects

Subject disposition will be presented in terms of the numbers and percentages of subjects who were randomized, completed the study, and discontinued from the study. Subjects who are not discontinued from the study will be considered study completers. Disposition will be summarized by treatment group and for all subjects.

The number of subjects in each of the analysis populations (mITT, mITT2, PP and Safety) will be displayed by treatment and percentages will be calculated using randomized subjects as the denominator.

The number and percentage of subjects prematurely discontinued from the study and the reasons for study discontinuation will be summarized by treatment group for all randomized subjects. The reasons for study discontinuation that will be summarized include: subject choice, AE, protocol violations, administrative reasons, sponsor termination of study, and other. A subject listing will be provided that includes the date of and reason for premature study discontinuation.

The number and percentage of subjects with major protocol deviations will be summarized by treatment group for all randomized subjects. The protocol deviations that will be summarized include: informed consent, inclusion / exclusion and randomization, test article / study drug instillation and assignment at site, improper protocol procedures at site, site's failure to report SAE / AE, visit out of window, subject's non-compliance with test article / study drug, subject's use of prohibited concomitant medication, subject's failure to follow instructions, and other. A subject listing will be provided that includes the date

of the deviation, the deviation description and the classification of whether the deviation was judged to be major or minor.

In addition, subject listings will be provided that include informed consent date, inclusion and exclusion criteria violations, and exclusions from the PP population.

10. Demographic Variables

The demographic variables collected in this study include age, sex, race, ethnicity and iris color. Subjects who record more than one race will be grouped into a single category denoted as "Multiple Races". Demographic variables will be summarized for the mITT, mITT2 and Safety populations, separately.

Age (years) will be summarized, overall and by treatment, using continuous descriptive statistics. Age will also be categorized as follows: <65 years and ≥65 years. Age will be reported in years and calculated using the following formula:

Age = (informed consent date – date of birth) / 365.25 truncated as an integer

The number and percentage of subjects will be presented, overall and by treatment, for age category, sex, race, ethnicity and iris color. Iris color will be summarized for the right eye (OD), left eye (OS), and study eye separately.

A subject listing that includes all demographic variables will be provided.

11. Medical History and Concomitant Medications

11.1 Medical History

Medical history will be coded using MedDRA Version 21.0.

Non-ocular medical history will be summarized using discrete summary statistics and presented by treatment group at the subject and event level by System Organ Class (SOC) and Preferred Term (PT) using the mITT population. Ocular medical history will be similarly summarized at the subject level. If a subject reports the same PT multiple times within the same SOC, that PT will only be reported once within that SOC. As with the PT, if a subject reports multiple conditions within the same SOC, that SOC will only be reported once.

Listings of medical history will be generated separately for ocular and non-ocular data.

11.2 Concomitant Medications

Concomitant medications will be coded using World Health Organization (WHO) Drug Global B3 Dictionary March 2018 and summarized to the therapeutic drug class (Anatomical Therapeutic Chemical [ATC] 4 classification) and preferred name.

Concomitant medications are defined as those medications listed as having been taken 1) prior to initiation of study drug administration and continuing for any period of time following the first administration of study drug or 2) at any time following the first administration of study drug.

Concomitant medications will be summarized using the mITT population. Medications will be tabulated for each treatment group using frequencies and percentages. Subjects may have more than 1 medication per ATC text. At each level of subject summarization, a subject will be counted once if he/she reports 1 or more medications. Percentages will be based on the number of subjects in each treatment group. Listings of concomitant medications will be generated separately for ocular and non-ocular data.

12. Dosing Compliance and Treatment Exposure

12.1 Dosing Compliance

Dosing compliance (% compliance) will be assessed by calculating the number of actual doses received and comparing that to the number of expected doses as follows:

$$\text{Compliance (\%)} = \frac{\text{Number of Actual Doses Received}}{\text{Number of Expected Doses}} \times 100\%$$

The number of actual doses received will be calculated from the number of used vials recorded in the CRF after Visit 2 (Day 1). The number of expected doses that will be used for calculating compliance will be calculated as 2x[(date of completion/discontinuation – date of Visit 2 [Day 1]) +1] for all subjects with BID dosing. For subjects with TID dosing, the number of expected doses will be calculated as 3x[(date of completion/discontinuation – date of Visit 2 [Day 1]) +1].

A categorical dosing compliance variable will also be derived as non-compliant (<80% or >125%) and compliant (≥80% and ≤125%).

Dosing compliance (%) will be summarized with continuous descriptive statistics for each treatment group, using the mITT and mITT2 populations. The compliance category defined above will be summarized with discrete summary statistics.

A subject listing of dosing compliance will also be produced.

12.2 Treatment Exposure

Extent of treatment exposure for all subjects will be calculated in days using the following:

Extent of Exposure (days) = (Date of completion/discontinuation – date of Visit 2 [Day 1]) + 1

Extent of treatment exposure (days) for each subject exposed to study drug will be summarized with continuous descriptive statistics for each treatment group, using the Safety population. A subject listing of treatment exposure will also be produced.

13. Efficacy Analyses

13.1 Primary Analysis

The primary efficacy variables (Pre-CAE®) are:

- Change from Baseline to Visit 5 (Day 85 ± 2) in inferior corneal staining score (Ora Calibra® scale) in the study eye
- Change from Baseline to Visit 5 (Day 85 ± 2) in total corneal staining score (Ora Calibra® scale) in the study eye
- Change from Baseline to Visit 5 (Day 85 ± 2) in total corneal staining score (Oxford scale) in the study eye
- Change from Baseline to Visit 5 (Day 85 ± 2) in eye dryness measured using VAS, and
- Change from Baseline to Visit 5 (Day 85 ± 2) in Total OSDI score

For each endpoint, change from baseline will be calculated as visit minus baseline such that a positive difference indicates a worsening of dry eye signs or symptoms. In addition, treatment comparisons between active and vehicle will be calculated as active minus vehicle, such that a negative result indicates a better score for the active treatment (i.e., the active treatment had a smaller increase in dry eye signs or symptoms than the placebo group). For comparisons between active and vehicle, dosing (TID or BID) of the vehicle will match the dosing of the active treatment.

13.1.1 Pre-CAE® Inferior Fluorescein Staining (Ora Calibra® scale)

Pre-CAE® fluorescein staining in the inferior region of the cornea will be graded using the Ora Calibra® Corneal and Conjunctival Staining Scale. The Ora Calibra® Corneal and Conjunctival Staining Scale ranges from 0 to 4 (half grade increments may be used), where grade 0 = none, 1 = trace, 2 = mild, 3 = moderate, and 4 = severe.

Changes from baseline in the pre-CAE® inferior fluorescein staining scores will be summarized at Visit 5 (Day 85 ± 2) by treatment group for the study eye using quantitative summary statistics. Changes from baseline will be compared between each AXR-159 Ophthalmic Solution group versus vehicle group at matched dosing frequency (TID or BID) using an ANCOVA model that adjusts for baseline. Specifically, the ANCOVA model will include terms for baseline inferior corneal staining score (ICCS) and baseline eye dryness score as covariates and treatment group as a factor in the model. The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. Pairwise t-tests from the ANCOVA model will be used to compare treatment and vehicle groups.

The following SAS code will be used to run the ANCOVA analysis for each of Stage 1 and Stage 2:

```
PROC MIXED DATA = INDATA;
```

```
        CLASS TREATMENT;
        MODEL CHANGE_ICSS = BASELINE_ICSS BASELINE_EDS TREATMENT
              / SOLUTION COVB;
        LSMEANS TREATMENT / CL PDIFF;
        ODS OUTPUT LSMEANS = OUTLS DIFFS = OUTDIFFS;
RUN;
```

where

- *TREATMENT* is the name of the treatment group variable
- *BASELINE_ICSS* is the baseline pre-CAE® inferior fluorescein staining score in the study eye
- *BASELINE_EDS* is the baseline pre-CAE® eye dryness score
- *CHANGE_ICSS* is the pre-CAE® inferior fluorescein staining in the study eye at Visit 5 (Day 85 ± 2) – *BASELINE_ICSS*
- *OUTLS* is the name of the output dataset that contains the statistical results for the treatment means from the ANCOVA model
- *OUTDIFFS* is the name of the output dataset that contains the statistical results for the differences in treatment means from the ANCOVA model

T-tests and Wilcoxon rank sum tests will also be conducted as sensitivity analyses to assess robustness of the results.

The primary analysis will be performed on the mITT population with the LOCF imputation method for missing values. For the LOCF analysis, the last value from the previous visits will be carried forward. Only pre-CAE® or non-CAE® time points will be used to impute a missing pre-CAE® value.

As sensitivity analyses, the primary analysis will also be performed on the mITT2 population with LOCF, the PP population with LOCF, the mITT population with observed data only, and the mITT population with MCMC imputation.

The MCMC method will be performed using the SAS procedure PROC MI. The SAS code for obtaining multiple imputation data is:

```
PROC MI DATA = INDATA SEED = SEED_VALUE OUT = OUTDATA NIMPUTE = 20
             MINIMUM = 0 MAXIMUM = 4 ROUND = 0.5;
        BY TREATMENT
        MCMC INITIAL = EM;
        VAR BASELINE_ICSS ICSS;
RUN;
```

where

- *INDATA* is the name of the input dataset
- *OUTDATA* is the name of the output dataset

- *TREATMENT* is the name of the treatment group variable
- *BASELINE_ICSS* is the baseline pre-CAE® inferior fluorescein staining score in the study eye
- *ICSS* is the pre-CAE® inferior fluorescein staining in the study eye at Visit 5 (Day 85 ± 2)

In the above, the random number seed SEED_VALUE will be set to 62521 + S, where S = 1 for Stage 1 data analysis, S = 2 for Stage 2 data analysis, and S = 3 for analysis of the combined Stage 1 and Stage 2 data.

After obtaining twenty complete data sets and calculating changes from baseline, the following SAS code will be used to run the ANCOVA model on each data set and combine the results from the twenty analyses:

```
PROC MIXED DATA = OUTDATA;
       BY _IMPUTATION_;
       CLASS TREATMENT;
       MODEL CHANGE_ICSS = BASELINE_ICSS BASELINE_EDS TREATMENT
              / SOLUTION COVB;
       LSMEANS TREATMENT / CL PDIFF;
       ODS OUTPUT LSMEANS = OUTLS DIFFS = OUTDIFFS;
RUN;
PROC SORT DATA=OUTLS; BY TREATMENT _IMPUTATION_; RUN;
PROC MIANALYZE DATA=OUTLS;
       BY TREATMENT;
       MODELEFFECTS ESTIMATE;
       STDERR STDERR;
RUN;

DATA OUTDIFFS;
       SET OUTDIFFS;
       COMPARISON = TREATMENT||' - '||LEFT(_TREATMENT);
RUN;
PROC SORT DATA=OUTDIFFS; BY COMPARISON _IMPUTATION_; RUN;
PROC MIANALYZE DATA=OUTDIFFS;
       BY COMPARISON;
       MODELEFFECTS ESTIMATE;
       STDERR STDERR;
RUN;
```

where

- *TREATMENT* is the name of the treatment group variable
- *BASELINE_ICSS* is the baseline pre-CAE® inferior fluorescein staining score in the study eye
- *BASELINE_EDS* is the baseline pre-CAE® eye dryness score
- *CHANGE_ICSS* is the pre-CAE® inferior fluorescein staining in the study eye at Visit 5 (Day 85 ± 2) – *BASELINE_ICSS*

- *OUTLS* is the name of the output dataset that contains the statistical results for the treatment means from the ANCOVA model that is run on each of the twenty imputation datasets
- *OUTDIFFS* is the name of the output dataset that contains the statistical results for the differences in treatment means from the ANCOVA model that is run on each of the twenty imputation datasets

Similar SAS code will be used to conduct MCMC multiple imputation analysis for t-tests using the same imputation data sets generated above.

Pre-CAE® inferior fluorescein staining changes from baseline in the study eye will be displayed graphically in a bar chart with standard error bars by visit and treatment group based on the ANCOVA analysis.

13.1.2 PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE)

Pre-CAE® fluorescein staining will be graded using the Ora Calibra® Corneal and Conjunctival Staining Scale. The Ora Calibra® Corneal and Conjunctival Staining Scale ranges from 0 to 4 (half grade increments may be used), where grade 0 = none, 1 = trace, 2 = mild, 3 = moderate, and 4 = severe. Staining will be graded in the inferior, superior, corneal, temporal and nasal regions. The total corneal fluorescein staining score is the sum of the scores from the inferior, corneal and superior regions.

Pre-CAE® total corneal fluorescein staining will be analyzed similarly to pre-CAE® inferior fluorescein staining. Pre-CAE® total corneal fluorescein staining changes from baseline in the study eye will be displayed graphically in a bar chart with standard error bars by visit and treatment group based on the ANCOVA analysis. The ANCOVA models, including the ANCOVA model used in the MCMC analysis, will include terms for baseline total corneal staining score, baseline ICCS and baseline eye dryness score as covariates and treatment group as a factor in the model.

LOCF and MCMC imputation will be performed for each region separately, prior to calculating the total corneal fluorescein staining score. The following random number seed values will be used for the MCMC imputations: 62521 + S for inferior region, 38751 + S for central region, 91121 + S for superior region, 22252 + S for temporal region, and 83620 + S for nasal region, where S = 1 for Stage 1 data analysis, S = 2 for Stage 2 data analysis, and S = 3 for analysis of the combined Stage 1 and Stage 2 data.

13.1.3 PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE)

The Oxford scale ranges from 0 to 5 for the corneal region with higher scores indicating greater staining.

Pre-CAE® total corneal fluorescein staining (Oxford scale) will be analyzed similarly to pre-CAE® inferior fluorescein staining (Ora Calibra® scale). The ANCOVA models, including the ANCOVA model used in

the MCMC analysis, will include terms for baseline total corneal staining score (Oxford scale), baseline inferior corneal staining score (Ora Calibra® scale) and baseline eye dryness score as covariates and treatment group as a factor in the model. Pre-CAE® total corneal fluorescein staining changes from baseline in the study eye will be displayed graphically in a bar chart with standard error bars by visit and treatment group based on the ANCOVA analysis.

The random number seed values that will be used for the MCMC imputations are given by 61521 + S, where S = 1 for Stage 1 data analysis, S = 2 for Stage 2 data analysis, and S = 3 for analysis of the combined Stage 1 and Stage 2 data.

13.1.4 PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE)

In the VAS assessment, the subject will be asked to rate each of several ocular symptoms due to ocular dryness by placing a vertical mark on a 100 mm horizontal line to indicate the level of discomfort. A score of 0 corresponds to “no discomfort” and 100 corresponds to “maximal discomfort”.

Eye dryness will be assessed by VAS and analyzed similarly to pre-CAE® inferior fluorescein staining (Ora Calibra® scale). The ANCOVA models, including the ANCOVA model used in the MCMC analysis, will include terms for baseline eye dryness (VAS) and baseline inferior corneal staining score (Ora Calibra® scale) as covariates and treatment group as a factor in the model. Eye dryness changes from baseline will be displayed graphically in a bar chart with standard error bars by visit and treatment group based on the ANCOVA analysis.

The random number seed values that will be used for the MCMC imputations are given by 65521 + S, where S = 1 for Stage 1 data analysis, S = 2 for Stage 2 data analysis, and S = 3 for analysis of the combined Stage 1 and Stage 2 data.

13.1.5 PRE-CAE® TOTAL OSDI

The OSDI© is assessed on a scale of 0 to 100, with higher scores representing greater disability. The OSDI© asks the following 12 questions at the subject level:

Have you experienced any of the following during the last week:

1) Eyes that are sensitive to light?
2) Eyes that feel gritty?
3) Painful or sore eyes?
4) Blurred vision?
5) Poor vision?

Have problems with your eyes limited you in performing any of the following during the last week:

6) Reading?
7) Driving at night?
8) Working with a computer or bank machine (ATM)?

9) Watching TV?

Have your eyes felt uncomfortable in any of the following situations during the last week:

10) Windy conditions?
11) Places or areas with low humidity (very dry)?
12) Areas that are air conditioned?

OSDI© will be collected for both eyes pre-CAE® at each visit. The 5-unit scale for responses to the OSDI© is given by the following: 0 = None of the time, 1 = Some of the time, 2 = Half of the time, 3 = Most of the time and 4 = All of the time. The total OSDI© score is calculated by the following:

$$\text{OSDI©} = \frac{\text{(sum of scores) x 25}}{\text{\# of questions answered}}$$

Note that the number of questions answered in the denominator should exclude those questions with a response of "N/A".

Pre-CAE® Total OSDI© will be analyzed similarly to pre-CAE® inferior fluorescein staining (Ora Calibra® scale). The ANCOVA models, including the ANCOVA model used in the MCMC analysis, will include terms for baseline Total OSDI©, baseline inferior corneal staining score (Ora Calibra® scale) and baseline eye dryness score as covariates and treatment group as a factor in the model. Pre-CAE® Total OSDI© changes from baseline will be displayed graphically in a bar chart with standard error bars by visit and treatment group based on the ANCOVA analysis.

LOCF and MCMC imputation will be performed for total OSDI score; separate imputations will not be created for each individual question score. The random number seed values that will be used for the MCMC imputations are given by 67521 + S, where S = 1 for Stage 1 data analysis, S = 2 for Stage 2 data analysis, and S = 3 for analysis of the combined Stage 1 and Stage 2 data.

13.2 Secondary Analyses

The continuous and ordinal secondary efficacy variables collected at each visit will be summarized descriptively (n, mean, SD, median, min and max) by visit and treatment group. Change scores from pre- to post-CAE® will be calculated as post-CAE® score minus pre-CAE® score. Changes from baseline will also be summarized descriptively by visit and treatment group. No imputation will be performed for secondary efficacy variables. Analyses will be performed on the mITT population with observed data only. All secondary measures will also be presented in subject listings.

The following secondary efficacy endpoints will be tested:

- Unanesthetized Schirmer's Test
- TFBUT

- Conjunctival Redness Score
- Fluorescein Corneal Staining (Ora Calibra® scale)
- Fluorescein Corneal Staining (Oxford scale)
- Lissamine Green Conjunctival Staining (Oxford scale)
- Ocular Discomfort Score
- Ocular Discomfort & 4-Symptom Questionnaire
- VAS
- OSDI
- SANDE

13.2.1 UNANESTHETIZED SCHIRMER'S TEST

Unanesthetized Schirmer's Test will be assessed on both eyes at all visits. Visit 1 and 5 assessments will be pre-CAE®. The Schirmer's test strip will be placed in the lower temporal lid margin of each eye. After 5 minutes, the test strip will be removed and the length of the moistened area will be recorded in millimeters (mm) for each eye. Lower values indicate less tears produced in the eye.

Unanesthetized Schirmer's Test will be summarized by treatment group and visit using quantitative summary statistics. Change from baseline will be also summarized.

Pairwise two-sample t-tests will be employed to compare treatment and vehicle means at each visit and time point. The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Changes from baseline will be compared between treatment groups using ANCOVA models that adjust for baseline value, baseline inferior corneal staining (Ora Calibra® scale) and baseline eye dryness (VAS). The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. T-tests and Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Binary clinical cure variables will be defined by visit for Schirmer's test ≥ 5 mm, Schirmer's test ≥ 10 mm and Schirmer's change from baseline ≥ 5 mm, and will summarized by visit using number of subjects, frequency counts and percentages. Treatment groups will be compared pairwise with vehicle using Pearson's chi-square test or Fisher's exact test if the expected cell count is less than 5 in 25% or more of the cells. In addition, the proportion of responders will be compared between treatment groups using the Cochran-Mantel-Haenszel method stratifying by baseline ICSS (≤ 1.5, > 1.5) and baseline eye dryness (< 60, ≥ 60). For the Cochran-Mantel-Haenszel analysis of the combined Stage 1 and Stage 2 data, the study Stage will also be included as a stratification factor.

13.2.2 TEAR FILM BREAK-UP TIME (TFBUT)

TFBUT will be measured at all scheduled visits on both eyes. Both pre- and post-CAE® assessments will be made at Visits 1 and 5. For each eye, two measurements will be recorded in seconds and averaged unless the two measurements are >2 seconds apart and are each <10 seconds, in which case, a third measurement will be taken and the two closest of the three will be averaged and used for analyses. If the differences between two sequential pairs of measurements are the same, e.g., 3, 6, 9 seconds, then the median of the three readings will be used for analysis.

TFBUT will be summarized by treatment group, visit and time point (pre- and post-CAE®) using quantitative summary statistics. Change from baseline will be also summarized.

Pairwise two-sample t-tests will be employed to compare treatment and vehicle means at each visit and time point. The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Changes from baseline will be compared between treatment groups using ANCOVA models that adjust for baseline value, baseline inferior corneal staining (Ora Calibra® scale) and baseline eye dryness (VAS). The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. T-tests and Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Binary clinical cure variables will be defined by visit for TFBUT ≥ 5 s, TFBUT ≥ 10 s, and TFBUT change from baseline ≥ 5 s, and will be summarized by visit using number of subjects, frequency counts and percentages. Treatment groups will be compared pairwise with vehicle using Pearson's chi-square test or Fisher's exact test if the expected cell count is less than 5 in 25% or more of the cells. In addition, the proportion of responders will be compared between treatment groups using the Cochran-Mantel-Haenszel method stratifying by baseline ICSS (≤ 1.5, > 1.5) and baseline eye dryness (< 60, ≥ 60). For the Cochran-Mantel-Haenszel analysis of the combined Stage 1 and Stage 2 data, the study Stage will also be included as a stratification factor.

13.2.3 OCULUS KERATOGRAPH

Oculus keratography will be assessed at all visits at selected sites only. Only pre-CAE® assessments will be made at Visits 1 and 5. First break (seconds), average time (seconds) and tear meniscus height (mm) will be recorded.

Oculus keratography measurements will be summarized by treatment group and visit using quantitative summary statistics. Change from baseline will be also summarized.

Pairwise two-sample t-tests will be employed to compare treatment and vehicle means at each visit and time point. The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Changes from baseline will be compared between treatment groups using ANCOVA models that adjust for baseline value, baseline inferior corneal staining (Ora Calibra® scale) and baseline eye dryness (VAS). The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. T-tests and Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

13.2.4 CONJUNCTIVAL REDNESS SCORE

The Ora Calibra® Conjunctival Redness Scale for Dry Eye will be performed on all scheduled visits. Both pre- and post-CAE® assessments will be made at Visits 1 and 5. The conjunctival redness scale ranges from 0 to 4 where 0 = normal, without vasodilation, 1 = trace ciliary or conjunctival vasodilation, 2 = broad ciliary vasodilation, 3 = broad ciliary and slight, horizontal conjunctival vasodilation, and 4 = broad ciliary and prominent, horizontal conjunctival vasodilation. Half unit increments are allowed.

Conjunctival redness will be summarized by treatment group, visit and time point (pre- and post-CAE®) using quantitative summary statistics. Change from baseline will be also summarized.

Pairwise two-sample t-tests will be employed to compare treatment and vehicle means at each visit and time point. The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Changes from baseline will be compared between treatment groups using ANCOVA models that adjust for baseline value, baseline inferior corneal staining (Ora Calibra® scale) and baseline eye dryness (VAS). The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. T-tests and Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

A binary clinical cure variable will be defined by visit for conjunctival redness = 0, and will be summarized by visit using number of subjects, frequency counts and percentages. Treatment groups will be compared pairwise with vehicle using Pearson's chi-square test or Fisher's exact test if the expected cell count is less than 5 in 25% or more of the cells. In addition, the proportion of responders will be compared between treatment groups using the Cochran-Mantel-Haenszel method stratifying by baseline ICSS (≤ 1.5, > 1.5) and baseline eye dryness (< 60, ≥ 60). For the Cochran-Mantel-Haenszel

analysis of the combined Stage 1 and Stage 2 data, the study Stage will also be included as a stratification factor.

13.2.5 FLUORESCEIN CORNEAL STAINING (ORA CALIBRA® SCALE)

Corneal and conjunctival fluorescein staining will be performed at all scheduled visits, on both eyes and graded using the Ora Calibra® Corneal and Conjunctival Staining Scale. Both pre- and post-CAE® assessments will be made at Visits 1 and 5. The scale will grade the cornea and conjunctiva by five regions: inferior, superior, central, temporal, and nasal. The Ora Calibra® Corneal and Conjunctival Staining Scale ranges from 0 to 4 (half grade increments may be used), where grade 0 = none, 1 = trace, 2 = mild, 3 = moderate, and 4 = severe.

Fluorescein staining scores will be summarized by treatment group, visit, time point (pre- and post-CAE®), and region (5 regions, plus corneal sum, conjunctival sum, and total scores) for the study eye using quantitative summary statistics. The corneal sum score will be the sum of scores from the inferior, superior, and central regions. The conjunctival sum score will be the sum of scores from the nasal and temporal regions. The total score will be the sum of scores from all five regions.

Pairwise two-sample t-tests will be employed to compare treatment and vehicle means at each visit and time point. The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Changes from baseline will be compared between treatment groups using ANCOVA models that adjust for baseline value, baseline inferior corneal staining (Ora Calibra® scale) and baseline eye dryness (VAS). The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. T-tests and Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Binary clinical cure variables will be defined by visit and region for clearing (score = 0) and 1-unit improvement (change from baseline <= -1), and will be summarized by visit and region using number of subjects, frequency counts and percentages. Treatment groups will be compared pairwise with vehicle using Pearson's chi-square test or Fisher's exact test if the expected cell count is less than 5 in 25% or more of the cells. In addition, the proportion of responders will be compared between treatment groups using the Cochran-Mantel-Haenszel method stratifying by baseline ICSS (≤ 1.5, > 1.5) and baseline eye dryness (< 60, ≥ 60). For the Cochran-Mantel-Haenszel analysis of the combined Stage 1 and Stage 2 data, the study Stage will also be included as a stratification factor.

13.2.6 FLUORESCEIN CORNEAL STAINING (OXFORD SCALE)

Corneal fluorescein staining will be performed at all scheduled visits and graded using the Oxford Scale. Both pre- and post-CAE® assessments will be made at Visits 1 and 5. The Oxford scale for corneal staining ranges from 0 to 5 for the corneal region. with higher scores indicating greater staining.

Staining scores will be summarized by treatment group, visit and time point (pre- and post-CAE®) using quantitative summary statistics. Change from baseline will be also summarized. Each region and total score will be summarized separately.

Pairwise two-sample t-tests will be employed to compare treatment and vehicle means at each visit and time point. The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Changes from baseline will be compared between treatment groups using ANCOVA models that adjust for baseline value, baseline inferior corneal staining (Ora Calibra® scale) and baseline eye dryness (VAS). The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. T-tests and Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Binary clinical cure variables will be defined by visit and region for clearing (score = 0) and 1-unit improvement (change from baseline <= -1), and will be summarized by visit and region using number of subjects, frequency counts and percentages. Treatment groups will be compared pairwise with vehicle using Pearson's chi-square test or Fisher's exact test if the expected cell count is less than 5 in 25% or more of the cells. In addition, the proportion of responders will be compared between treatment groups using the Cochran-Mantel-Haenszel method stratifying by baseline ICSS (≤ 1.5, > 1.5) and baseline eye dryness (< 60, ≥ 60). For the Cochran-Mantel-Haenszel analysis of the combined Stage 1 and Stage 2 data, the study Stage will also be included as a stratification factor.

13.2.7 LISSAMINE GREEN CONJUNCTIVAL STAINING (OXFORD SCALE)

Lissamine green conjunctival staining will be performed at all scheduled visits and graded using the Oxford Scale. The Oxford scale for conjunctival staining ranges from 0 to 5 for each of the nasal and temporal regions, with higher scores indicating greater staining. The total conjunctival score is the sum of the two regions and ranges from 0 to 10.

Staining scores will be summarized by treatment group, visit and time point (pre- and post-CAE®) using quantitative summary statistics. Change from baseline will be also summarized. Each region and total score will be summarized separately.

Pairwise two-sample t-tests will be employed to compare treatment and vehicle means at each visit and time point. The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Changes from baseline will be compared between treatment groups using ANCOVA models that adjust for baseline value, baseline inferior corneal staining (Ora Calibra® scale) and baseline eye dryness (VAS). The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. T-tests and Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Binary clinical cure variables will be defined by visit and region for clearing (score = 0) and 1-unit improvement (change from baseline <= -1), and will be summarized by visit and region using number of subjects, frequency counts and percentages. Treatment groups will be compared pairwise with vehicle using Pearson's chi-square test or Fisher's exact test if the expected cell count is less than 5 in 25% or more of the cells. In addition, the proportion of responders will be compared between treatment groups using the Cochran-Mantel-Haenszel method stratifying by baseline ICSS (≤ 1.5, > 1.5) and baseline eye dryness (< 60, ≥ 60). For the Cochran-Mantel-Haenszel analysis of the combined Stage 1 and Stage 2 data, the study Stage will also be included as a stratification factor.

13.2.8 Ocular Discomfort Score

Ocular discomfort scores will be subjectively graded by the subjects using the Ora Calibra® Ocular Discomfort Scale at all scheduled visits. Both pre- and post-CAE® assessments will be made at Visits 1 and 5. Ocular discomfort scores will also be assessed during the CAE® exposure, immediately upon entering the chamber and every 5 minutes thereafter for the duration of the 90 minute exposure. The ocular discomfort scale ranges from 0 to 4 where 0 = no discomfort, 1 = intermittent awareness, 2 = constant awareness, 3 = intermittent discomfort, and 4 = constant discomfort.

13.2.8.1 Ora Calibra® Ocular Discomfort Scale Pre-, Post-, and Non-CAE®

Pre- and post-CAE® assessments of ocular discomfort will be made at Visits 1 and 5. Ocular discomfort will also be assessed during the non-CAE Visits 2, 3, and 4. Ocular discomfort will be summarized by treatment group, visit and time point (pre- and post-CAE®) using quantitative summary statistics. Change from baseline will be also summarized.

Pairwise two-sample t-tests will be employed to compare treatment and vehicle means at each visit and time point. The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Changes from baseline will be compared between treatment groups using ANCOVA models that adjust for baseline value, baseline inferior corneal staining (Ora Calibra® scale) and baseline eye dryness (VAS). The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. T-tests and Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

A binary clinical cure variable will be defined by visit for pre-CAE® ocular discomfort score = 0, and summarized by visit using number of subjects, frequency counts and percentages. Treatment groups will be compared pairwise with vehicle using Pearson's chi-square test or Fisher's exact test if the expected cell count is less than 5 in 25% or more of the cells. In addition, the proportion of responders will be compared between treatment groups using the Cochran-Mantel-Haenszel method stratifying by baseline ICSS (≤ 1.5, > 1.5) and baseline eye dryness (< 60, ≥ 60). For the Cochran-Mantel-Haenszel analysis of the combined Stage 1 and Stage 2 data, the study Stage will also be included as a stratification factor.

13.2.8.2 Ora Calibra® Ocular Discomfort Scale During CAE® Exposure

Ocular discomfort scores will be assessed every 5 minutes during the CAE® exposure. Continuous descriptive statistics, including 95% CIs, as well as changes from baseline will be summarized by treatment group, visit, and time point. The change from the 0 minutes assessment within the same visit and changes from baseline will also be summarized by treatment group, visit, and time point.

For both the ocular discomfort score and the change from 0 minutes, pairwise two-sample t-tests will be employed to compare treatment and vehicle means at each visit and time point. The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Changes from baseline will be compared between treatment groups using ANCOVA models that adjust for baseline value, baseline inferior corneal staining (Ora Calibra® scale) and baseline eye dryness (VAS). The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. T-tests and Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

13.2.9 Ora Calibra® Ocular Discomfort & 4-Symptom Questionnaire

Ocular discomfort and dry eye symptoms will be assessed at all scheduled visits at the subject level in regard to how both eyes feel. Both pre- and post-CAE® assessments will be made at Visits 1 and 5. The Ora Calibra® Ocular Discomfort & 4-Symptom Questionnaire will be used, which includes rating of the severity of 5 symptoms: ocular discomfort, burning, dryness, grittiness, and stinging. Each symptom rating ranges from 0 to 5, where 0 = none and 5 = worst.

Symptom scores will be summarized by visit, time point, and treatment group using quantitative summary statistics, including 95% CIs. Change from baseline will also be summarized.

Pairwise two-sample t-tests will be employed to compare treatment and vehicle means at each visit and time point. The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Changes from baseline will be compared between treatment groups using ANCOVA models that adjust for baseline value, baseline inferior corneal staining (Ora Calibra® scale) and baseline eye dryness (VAS). The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. T-tests and Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

13.2.10 Visual Analog Scale

At every visit, subjects will be asked to rate each ocular symptom due to ocular dryness by placing a vertical mark on a horizontal line of length 100 mm to indicate the level of discomfort. 0 mm corresponds to “no discomfort” and 100 mm corresponds to “maximal discomfort.” Both pre- and post-CAE® assessments will be made at Visits 1, 2, 4, and 5. Symptoms assessed are burning/stinging, itching, foreign body sensation, blurred vision, eye dryness, photophobia, and pain.

Symptom scores and the average symptom score will be summarized by visit, time point, and treatment group using quantitative summary statistics, including 95% CIs. Change from baseline will also be summarized.

Pairwise two-sample t-tests will be employed to compare treatment and vehicle means at each visit and time point. The differences in means, two-sided 95% CI for the difference in means and p-values will be reported. Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Changes from baseline will be compared between treatment groups using ANCOVA models that adjust for baseline value, baseline inferior corneal staining (Ora Calibra® scale) and baseline eye dryness (VAS). The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. T-tests and Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

13.2.11 Ocular Surface Disease Index (OSDI)

The OSDI is described in Section 13.1.5. OSDI will be assessed on both eyes at all visits. Visit 1 and 5 assessments will be pre-CAE®. OSDI will be summarized by treatment group and visit using

quantitative summary statistics. Change from baseline will be also summarized. Each individual response, subtotal scores, and total OSDI score will be presented separately.

Pairwise two-sample t-tests will be employed to compare treatment and vehicle means at each visit and time point. The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Changes from baseline will be compared between treatment groups using ANCOVA models that adjust for baseline value, baseline inferior corneal staining (Ora Calibra® scale) and baseline eye dryness (VAS). The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. T-tests and Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

A binary clinical cure variable will be defined by visit for Total OSDI < 18, and summarized by visit using number of subjects, frequency counts and percentages. Treatment groups will be compared pairwise with vehicle using Pearson's chi-square test or Fisher's exact test if the expected cell count is less than 5 in 25% or more of the cells. In addition, the proportion of responders will be compared between treatment groups using the Cochran-Mantel-Haenszel method stratifying by baseline ICSS (≤ 1.5, > 1.5) and baseline eye dryness (< 60, ≥ 60). For the Cochran-Mantel-Haenszel analysis of the combined Stage 1 and Stage 2 data, the study Stage will also be included as a stratification factor.

13.2.12 Symptom Assessment in Dry Eye (SANDE)

The SANDE Questionnaire will be assessed on both eyes at all visits. Visit 1 and 5 assessments will be pre-CAE®. In this questionnaire, subjects indicate the frequency that their eyes feel dry and/or irritated and the severity of their symptoms. Frequency is measured on a 0-100 mm scale with 0 indicating rarely and 100 indicating all the time. Severity is also measured on a 0-100 mm scale with 0 indicating very mild and 100 indicating very severe. The SANDE Score is calculated as the product of the square root of the Frequency Score and the square root of the Severity Score.

The Frequency, Severity and combined SANDE Scores will be summarized by treatment group and visit using quantitative summary statistics. Change from baseline will be also summarized.

Pairwise two-sample t-tests will be employed to compare treatment and vehicle means at each visit and time point. The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Changes from baseline will be compared between treatment groups using ANCOVA models that adjust for baseline value, baseline inferior corneal staining (Ora Calibra® scale) and baseline eye dryness

(VAS). The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. T-tests and Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

14. Exploratory Analyses

No exploratory analyses are planned.

15. Subgroup Analyses

Patients will be stratified by the Pre-CAE® ICCS (i.e., ≤ 1.5 or > 1.5) according to the Ora Calibra® staining scale and eye dryness score (i.e., < 60 or ≥ 60) in the study eye.

Subgroup analyses are planned for the 4 groups defined by the 2 stratification factors (Pre-CAE®):

1. ICCS ≤ 1.5 according to the Ora Calibra® staining scale and eye dryness score < 60
2. ICCS ≤ 1.5 according to the Ora Calibra® staining scale and eye dryness score ≥ 60
3. ICCS > 1.5 according to the Ora Calibra® staining scale and eye dryness score < 60
4. ICCS > 1.5 according to the Ora Calibra® staining scale and eye dryness score ≥ 60.

Subgroup analyses will be conducted for corneal fluorescein staining (Ora Calibra® scale), corneal fluorescein staining (Oxford scale), VAS, and Total OSDI. Each endpoint will be summarized by subgroup, treatment group, visit and time point (where appropriate).

Additional subgroup analyses will be conducted based upon strata defined by median baseline values in pre-CAE assessments. For each endpoint, separate analyses will be conducted for patients with pre-CAE baseline scores ≤ the pre-CAE baseline median, and for patients with pre-CAE baseline scores > the pre-CAE baseline median. These subgroup analyses will be conducted for all efficacy endpoints.

Subgroup analyses of symptom endpoints will also be conducted for the following two groups:

1. Patients with time to CAE qualification ≤ 20 minutes
2. Patients with time to CAE qualification > 20 minutes

For each subgroup, pairwise two-sample t-tests will be employed to compare treatment and vehicle means at each visit and time point. The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

Changes from baseline will be compared between treatment groups using ANCOVA models that adjust for baseline value. The differences in means, two-sided 95% CIs for the difference in means and p-values will be reported. T-tests and Wilcoxon rank sum tests will also be conducted. Analyses will be performed on the mITT population with observed data only.

16. Safety Analyses

All safety analyses will be conducted using the Safety Population.

16.1 Adverse Events

An AE is defined as any untoward medical occurrence associated with the use of an IP in humans, whether or not considered IP-related. An AE can be any unfavorable and unintended sign (e.g., an abnormal laboratory finding), symptom, or disease temporally associated with the use of an IP, without any judgment about causality. An AE can arise from any use of the IP (e.g., off-label use, use in combination with another drug or medical device) and from any route of administration, formulation, or dose, including an overdose. An AE can arise from any delivery, implantation, or use of a medical device, including medical device failure, subject characteristics that may impact medical device performance (e.g., anatomical limitations), and therapeutic parameters (e.g., energy applied, sizing, dose release, and anatomic fit) associated with medical device use.

All AEs spontaneously reported by the subject and/or in response to an open question from study personnel or revealed by observation, physical examination or other diagnostic procedures will be recorded in the source document and on the appropriate pages of the case report form. Any clinically relevant deterioration in clinical finding is considered an AE and must be recorded. When possible, signs and symptoms indicating a common underlying pathology should be noted as one comprehensive event.

Documentation regarding the AE should be made as to the nature, date of onset, end date, severity, and relationship to IP, action(s) taken, seriousness, and outcome of any sign or symptom observed by the physician or reported by the subject upon indirect questioning.

Severity of an AE is defined as a qualitative assessment of the degree of intensity of an AE as determined by the investigator or reported to him/her by the subject. The assessment of severity is made irrespective of relationship to IP or seriousness of the event and should be evaluated according to the following scale:

- Mild: Event is noticeable to the subject, but is easily tolerated and does not interfere with the subject's daily activities.
- Moderate: Event is bothersome, possibly requiring additional therapy, and may interfere with the subject's daily activities.
- Severe: Event is intolerable, necessitates additional therapy or alteration of therapy, and interferes with the subject's daily activities.

A determination will be made of the relationship (if any) between an adverse event and the study drug or study procedure, as applicable. A causal relationship is present if a determination is made that

there is a reasonable possibility that the adverse event may have been caused by the drug or study procedure.

The relationship of each AE to the IP should be determined by the investigator using these explanations:

- ***Suspected*:** A reasonable possibility exists that the IP caused the AE. A suspected AE can be further defined as:
  - *Definite*: Relationship exists when the AE follows a reasonable sequence from the time of IP administration, follows a known response pattern of the drug class, is confirmed by improvement on stopping the IP and no other reasonable cause exists.
  - *Probable*: Relationship exists when the AE follows a reasonable sequence from the time of IP administration, follows a known response pattern of the drug class, is confirmed by improvement on stopping the IP and the suspect IP is the most likely of all causes.
  - *Possible*: Relationship exists when the AE follows a reasonable sequence from the time of IP administration, but could also have been produced by the subject's clinical state or by other drugs administered to the subject.
- ***Not Suspected:*** A reasonable possibility does not exist that the IP caused the AE.
  - *Not Related:* Concurrent illness, concurrent medication, or other known cause is clearly responsible for the AE, the administration of the IP and the occurrence of the AE are not reasonably related in time, OR exposure to IP has not occurred.

The expectedness of an AE should be determined based upon existing safety information about the IP using these explanations:

- Unexpected: An AE that is not listed in the Investigator's Brochure (IB) or is not listed at the specificity or severity that has been observed.
- Expected: An AE that is listed in the IB at the specificity and severity that has been observed.
- Not applicable: An AE unrelated to the IP.

AE events that are mentioned in the IB as occurring with a class of products or as anticipated from the pharmacological/mechanical (or other) properties of the product, but are not specifically mentioned as occurring with the particular product under investigation are to be considered unexpected.

The investigator should initially classify the expectedness of an AE, but the final classification is subject to the Medical Monitor's determination.

An AE is considered serious if, in the view of either the investigator or sponsor, it results in any of the following outcomes:

- Death;
- A life-threatening AE;

Note: An AE is considered "life-threatening" if, in the view of either the investigator or sponsor, its occurrence places the subject at immediate risk of death. It does not include an AE that, had it occurred in a more severe form, might have caused death.

The AE reporting period ends upon study exit. Study drug includes the investigational drug under evaluation and vehicle given during any stage of the study. All AEs will be coded using the MedDRA 21.0.

Treatment-emergent adverse events (TEAEs) are defined as any adverse event that occurs or worsens after the first dose of study treatment. AEs recorded in the eCRF which began prior to treatment will not be included in the summary tables but will be included in the AE data listings.

An overall summary will be presented that includes the number of AEs, TEAEs, serious AEs (SAE), and serious TEAEs (TE-SAE). The summary will also include the number and percentage of subjects withdrawn due to an AE, the number and percentage of subjects with an AE resulting in death, and the number and percentage of subjects who experienced at least one AE, TEAE, SAE and TE-SAE, by treatment group and for all subjects. This summary will include breakdowns of AEs further categorized as ocular or non-ocular. The summary will also include the number and percentage of resolved ocular AEs, and the mean number of days until AE resolution for resolved ocular AEs.

Additional summaries of TEAEs will be provided showing the number and percentage of subjects who experienced at least one TEAE. These summaries will be presented by SOC and PT. Non-ocular TEAEs will be summarized using discrete summary statistics and presented by treatment group at the subject and event level by SOC and PT. Ocular TEAEs will be similarly summarized at the subject and event level as well as for study and fellow eyes separately. If a subject reports the same PT multiple times within the same SOC, that PT will only be reported once within that SOC. As with the PT, if a subject reports multiple conditions within the same SOC, that SOC will only be reported once. In the summary, SOC will be listed in order of descending frequency for all subjects; PTs will be listed in order of descending frequency for all subjects within each SOC. The occurrence of non-ocular and ocular TEAEs will also be tabulated by SOC, PT, and maximal severity, as well as by study day of onset (prior to Day 15, Day 15 to Day 43, After Day 43).

Separate summaries will be provided for the following categories of AEs:

- Ocular TEAEs
- Non-ocular TEAEs
- Treatment-related ocular TEAEs
- Treatment-related non-ocular TEAEs
- SAEs

Summaries of TEAEs by maximal severity will be presented for ocular AEs and non-ocular AEs separately. The number of subjects with any TEAEs (along with percentages) will be tabulated by SOC and PT within each SOC by treatment group. To count the number of subjects with any TEAEs, if a subject has multiple TEAEs coded to the same PT within the same SOC, the subject will be counted once under the maximal severity.

All TEAEs with possible, probable, and definite relationship to IP are considered as treatment-related TEAEs.

All AEs will be presented in a subject listing that classifies each AE as ocular or non-ocular and indicates whether it is a TEAE. Separate listings will be produced for AEs leading to study discontinuation, AEs leading to death and SAEs.

16.2 Ora Calibra Drop Comfort Assessment

Ora Calibra® Drop Comfort Scale will be used at Visits 2, 4 and 5 to assess drop comfort for each eye separately upon instillation, and at 1 and 2 minutes post-instillation. The scale ranges from 0 to 10, with 0 indicating very comfortable and 10 indicating very uncomfortable. The scale will be summarized using continuous descriptive statistics by visit, time point and eye (study eye and fellow eye) for each treatment group.

Ora Calibra® Drop Comfort Questionnaire will be used to assess drop comfort 3 minutes post-instillation. Subjects will be asked to choose three words (among 12) that best describe how the eye drops feel in both eyes. The positive responses are comfortable, cool, refreshing, smooth, and soothing. The negative responses include burning, irritating, filmy, gritty, sticky, stinging, and thick. Subjects may also select “other” and write in a response of their choosing, which may be either a positive or a negative response. The results will be summarized for each response individually and for positive and negative responses using counts and percentages for each treatment group at each visit for each eye (study eye and fellow eye). Percentages will be based on the number of subjects in each treatment group with responses. A subject listing of the drop comfort assessment parameters will also be produced.

16.3 Best-corrected Visual Acuity (BCVA)

The visual acuity procedure will be performed at each visit pre-CAE®. The logarithm of the minimum angle of resolution (logMAR) VA must be assessed using an ETDRS chart. The procedure used will be

consistent with the recommendations provided for using the ETDRS eye chart. Visual Acuity should be evaluated at the beginning of each visit in the study (i.e., prior to slit-lamp examination). Subjects should use their most recent correction to attain their BCVA.

The observed and change from baseline visual acuity will be summarized for each eye (study eye and fellow eye) using continuous descriptive statistics by visit for each treatment group. A subject listing of visual acuity will also be produced.

16.4 Slit-lamp Biomicroscopy

A slit-lamp biomicroscopy examination of the cornea, conjunctiva, anterior chamber, iris, lens, and eyelid will be performed at each visit, and potentially at an Early Termination Visit. Both pre- and post-CAE® examinations will be made at Visits 1 and 5. The results will be graded as normal, Abnormal Not Clinically Significant (NCS) or Abnormal Clinically Significant (CS). Abnormal findings will be described.

The results will be summarized using counts and percentages for each treatment group at each visit for each eye (study eye and fellow eye). Percentages will be based on the number of subjects in each treatment group with responses. Shift tables for the slit-lamp biomicroscopy parameters will also be provided comparing each follow-up visit to Visit 1, Pre-CAE. A subject listing of the slit-lamp biomicroscopy parameters will also be produced.

16.5 Intraocular Pressure (IOP)

IOP will be measured in each eye by contact tonometry by the examiner and the results will be recorded in mmHg at all scheduled visits, and potentially at an Early Termination Visit. Assessments at Visits 1 and 5 will be post-CAE®. A single measurement is made to obtain a determination of IOP. The same tonometer employing the investigator's standard technique will be used throughout the study. In addition, all reasonable efforts will be made to have the same examiner obtain all IOP measurements for a given subject.

The IOP values and changes from baseline for each eye (study eye and fellow eye) will be summarized using continuous descriptive statistics by visit and eye for each treatment group and for all actively treated subjects. A subject listing of IOP will also be produced.

16.6 Ophthalmoscopy

Dilated fundus exams will be performed at Visit 1 using indirect ophthalmoscopy. At Visit 5, undilated fundus exams will be performed unless dilation is necessary. The investigator will make observations of the vitreous, retina, macula, choroid and optic nerve.

Observations will be graded as Normal or Abnormal. Abnormal findings that are clinically significant (as determined by the investigator that may interfere with study parameters or otherwise confound the data)

and those that are not clinically significant will be described. An indirect Fundoscopy examination should be performed if retinal disease is detected.

The results will be summarized using counts and percentages for each treatment group at each visit for each eye (study eye and fellow eye). Percentages will be based on the number of subjects in each treatment group with responses. Shift tables for the fundoscopy parameters will also be provided comparing Visit 5 to baseline (Visit 1). A subject listing of the fundoscopy parameters will also be produced.

16.7 Conjunctival Redness Score

The Ora Calibra® Conjunctival Redness Scale for Dry Eye will be performed on all scheduled visits. Both pre- and post-CAE® assessments will be made at Visits 1 and 5. The conjunctival redness scale ranges from 0 to 4 where 0 = normal, without vasodilation, 1 = trace ciliary or conjunctival vasodilation, 2 = broad ciliary vasodilation, 3 = broad ciliary and slight, horizontal conjunctival vasodilation, and 4 = broad ciliary and prominent, horizontal conjunctival vasodilation. Half unit increments are allowed.

Conjunctival redness will be summarized by treatment group, visit and time point (pre- and post-CAE®) using quantitative summary statistics. Change from baseline will be also summarized.

16.8 Vital Signs

Each subject will have vital signs assessments (resting blood pressure and pulse) conducted at Visits 1, 2, and 5. Vital signs are to be conducted by a qualified staff member who may be any of the following: a board-certified investigator or sub-investigator, nurse practitioner, registered nurse, or physician assistant.

Systolic and diastolic blood pressure should be measured in the same arm each time using a sphygmomanometer with the subjects who have been in a resting state (seated upright) at least 5 minutes. Blood pressure will be recorded in mmHg.

Pulse will be measured with the subjects who have been in a resting state (seated) for at least 5 minutes. Pulse will be counted for 30 seconds and multiplied by 2, and recorded in beats per minute (bpm).

The vital signs and changes from baseline will be summarized using continuous descriptive statistics by visit for each treatment group and for all actively treated subjects. A subject listing of vital signs will also be produced.

Vital signs will also be presented categorically for the number of subjects with low, normal, or high values as defined by the table below:

Vital Signs	Low	Normal	High
Systolic Blood Pressure (mmHg)	<90	90-180	>180

Vital Signs	Low	Normal	High
Diastolic Blood Pressure (mmHg)	<50	50-100	>100
Pulse Rate (bpm)	<50	50-110	>110

16.9 Laboratory Tests

Samples of blood (non-fasting) and urine will be collected at Visits 1 and 5 and evaluated for blood chemistry, hematology, and urinalysis. Parameters will be summarized using continuous descriptive statistics by visit for each treatment group and for all actively treated subjects. A subject listing will also be produced.

16.10 Urine Pregnancy Test

A urine pregnancy test will be conducted for females of childbearing potential at Visit 1 (Day -14 ± 2), Visit 5 (Day 85 ± 2), and may be conducted at an Unscheduled Visit. A listing of urine pregnancy test results will be generated.

17. Interim Analyses

An interim analysis will be performed when the last enrolled patient in Stage 1 completes Month 3 of the Expansion Cohort. There is no plan to stop the study for efficacy on the basis of the interim analysis. However, termination in individual dose groups due to safety, tolerability and/or futility may occur. Statistical significance will not be declared at the time of the interim analysis.

Given the exploratory nature of the study no Type I error adjustments will be made for the interim analysis including the Stage 1 data only.

18. Changes from Protocol-Stated Analyses

There are no changes from the protocol-stated analyses.

19. Revision History

The following revisions were made to SAP Version 2.0.

SAP Section	Revision	Rationale
12.1	Revised compliance calculation to use date of completion/discontinuation rather than date of last in-office instillation	Conservative estimation of compliance for discontinued subjects

12.2	Revised exposure calculation to use date of completion/discontinuation rather than date of last in-office instillation	Conservative estimation of exposure for discontinued subjects
13.1.1	Revised specification of random number seeds for MCMC	Consistency with 13.1.2
13.1.3, 13.1.4, 13.1.5	Revised specification of random number seeds for MCMC	Correction of seed specification

20. Tables

Tables that will be included in the topline delivery are shown in boldface font. Tables that will be included in the interim analysis are qualified as “Stage 1”.

Table Number	Title	Population
TABLE 14.1.1.1	SUBJECT DISPOSITION – STAGE 1	ALL RANDOMIZED SUBJECTS
TABLE 14.1.1.2	SUBJECT DISPOSITION – STAGE 2	ALL RANDOMIZED SUBJECTS
TABLE 14.1.1.3	**SUBJECT DISPOSITION – COMBINED STAGE 1 AND STAGE 2**	**ALL RANDOMIZED SUBJECTS**
TABLE 14.1.2.1.1	DEMOGRAPHICS – STAGE 1	MITT POPULATION
TABLE 14.1.2.1.2	DEMOGRAPHICS – STAGE 1	MITT2 POPULATION
TABLE 14.1.2.1.3	DEMOGRAPHICS – STAGE 1	SAFETY POPULATION
TABLE 14.1.2.2.1	DEMOGRAPHICS – STAGE 2	MITT POPULATION
TABLE 14.1.2.2.2	DEMOGRAPHICS – STAGE 2	MITT2 POPULATION
TABLE 14.1.2.2.3	DEMOGRAPHICS – STAGE 2	SAFETY POPULATION
TABLE 14.1.2.3.1	**DEMOGRAPHICS – COMBINED STAGE 1 AND STAGE 2**	**MITT POPULATION**
TABLE 14.1.2.3.2	DEMOGRAPHICS – COMBINED STAGE 1 AND STAGE 2	MITT2 POPULATION
TABLE 14.1.2.3.3	DEMOGRAPHICS – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.1.3.1.1	OCULAR MEDICAL HISTORY – STAGE 1	MITT POPULATION
TABLE 14.1.3.1.2	OCULAR MEDICAL HISTORY – STAGE 2	MITT POPULATION
TABLE 14.1.3.1.3	OCULAR MEDICAL HISTORY – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION
TABLE 14.1.3.2.1	NON-OCULAR MEDICAL HISTORY – STAGE 1	MITT POPULATION
TABLE 14.1.3.2.2	NON-OCULAR MEDICAL HISTORY – STAGE 2	MITT POPULATION
TABLE 14.1.3.2.3	NON-OCULAR MEDICAL HISTORY – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION

Table Number	Title	Population
TABLE 14.1.4.1.1	CONCOMITANT OCULAR MEDICATIONS BY TREATMENT GROUP, DRUG CLASS AND PREFERRED NAME – STAGE 1	MITT POPULATION
TABLE 14.1.4.1.2	CONCOMITANT OCULAR MEDICATIONS BY TREATMENT GROUP, DRUG CLASS AND PREFERRED NAME – STAGE 2	MITT POPULATION
TABLE 14.1.4.1.3	CONCOMITANT OCULAR MEDICATIONS BY TREATMENT GROUP, DRUG CLASS AND PREFERRED NAME – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION
TABLE 14.1.4.2.1	CONCOMITANT NON-OCULAR MEDICATIONS BY TREATMENT GROUP, DRUG CLASS AND PREFERRED NAME – STAGE 1	MITT POPULATION
TABLE 14.1.4.2.2	CONCOMITANT NON-OCULAR MEDICATIONS BY TREATMENT GROUP, DRUG CLASS AND PREFERRED NAME – STAGE 2	MITT POPULATION
TABLE 14.1.4.2.3	CONCOMITANT NON-OCULAR MEDICATIONS BY TREATMENT GROUP, DRUG CLASS AND PREFERRED NAME – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION
TABLE 14.2.1.1.1	PRE-CAE® INFERIOR CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 1	MITT POPULATION WITH LOCF
TABLE 14.2.1.1.2	PRE-CAE® INFERIOR CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 2	MITT POPULATION WITH LOCF
TABLE 14.2.1.1.3	**PRE-CAE® INFERIOR CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – COMBINED STAGE 1 AND STAGE 2**	**MITT POPULATION WITH LOCF**
TABLE 14.2.1.2.1	PRE-CAE® INFERIOR CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 1	MITT2 POPULATION WITH LOCF
TABLE 14.2.1.2.2	PRE-CAE® INFERIOR CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 2	MITT2 POPULATION WITH LOCF
TABLE 14.2.1.2.3	PRE-CAE® INFERIOR CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – COMBINED STAGE 1 AND STAGE 2	MITT2 POPULATION WITH LOCF
TABLE 14.2.1.3.1	PRE-CAE® INFERIOR CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 1	PP POPULATION WITH LOCF
TABLE 14.2.1.3.2	PRE-CAE® INFERIOR CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 2	PP POPULATION WITH LOCF
TABLE 14.2.1.3.3	PRE-CAE® INFERIOR CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – COMBINED STAGE 1 AND STAGE 2	PP POPULATION WITH LOCF
TABLE 14.2.1.4.1	PRE-CAE® INFERIOR CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.1.4.2	PRE-CAE® INFERIOR CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.1.4.3	PRE-CAE® INFERIOR CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.1.5.1	PRE-CAE® INFERIOR CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 1	MITT POPULATION WITH MCMC
TABLE 14.2.1.5.2	PRE-CAE® INFERIOR CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 2	MITT POPULATION WITH MCMC
TABLE 14.2.1.5.3	PRE-CAE® INFERIOR CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH MCMC
TABLE 14.2.2.1.1	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 1	MITT POPULATION WITH LOCF
TABLE 14.2.2.1.2	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 2	MITT POPULATION WITH LOCF

Table Number	Title	Population
TABLE 14.2.2.1.3	**PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – COMBINED STAGE 1 AND STAGE 2**	**MITT POPULATION WITH LOCF**
TABLE 14.2.2.2.1	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 1	MITT2 POPULATION WITH LOCF
TABLE 14.2.2.2.2	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 2	MITT2 POPULATION WITH LOCF
TABLE 14.2.2.2.3	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – COMBINED STAGE 1 AND STAGE 2	MITT2 POPULATION WITH LOCF
TABLE 14.2.2.3.1	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 1	PP POPULATION WITH LOCF
TABLE 14.2.2.3.2	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 2	PP POPULATION WITH LOCF
TABLE 14.2.2.3.3	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – COMBINED STAGE 1 AND STAGE 2	PP POPULATION WITH LOCF
TABLE 14.2.2.4.1	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.2.4.2	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.2.4.3	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.2.5.1	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 1	MITT POPULATION WITH MCMC
TABLE 14.2.2.5.2	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – STAGE 2	MITT POPULATION WITH MCMC
TABLE 14.2.2.5.3	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH MCMC
TABLE 14.2.3.1.1	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE) – STAGE 1	MITT POPULATION WITH LOCF
TABLE 14.2.3.1.2	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE) – STAGE 2	MITT POPULATION WITH LOCF
TABLE 14.2.3.1.3	**PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE) – COMBINED STAGE 1 AND STAGE 2**	**MITT POPULATION WITH LOCF**
TABLE 14.2.3.2.1	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE) – STAGE 1	MITT2 POPULATION WITH LOCF
TABLE 14.2.3.2.2	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE) – STAGE 2	MITT2 POPULATION WITH LOCF
TABLE 14.2.3.2.3	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE) – COMBINED STAGE 1 AND STAGE 2	MITT2 POPULATION WITH LOCF
TABLE 14.2.3.3.1	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE) – STAGE 1	PP POPULATION WITH LOCF
TABLE 14.2.3.3.2	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE) – STAGE 2	PP POPULATION WITH LOCF
TABLE 14.2.3.3.3	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE) – COMBINED STAGE 1 AND STAGE 2	PP POPULATION WITH LOCF
TABLE 14.2.3.4.1	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE) – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.3.4.2	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE) – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY

Table Number	Title	Population
TABLE 14.2.3.4.3	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE) – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.3.5.1	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE) – STAGE 1	MITT POPULATION WITH MCMC
TABLE 14.2.3.5.2	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE) – STAGE 2	MITT POPULATION WITH MCMC
TABLE 14.2.3.5.3	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE) - COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH MCMC
TABLE 14.2.4.1.1	PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE) – STAGE 1	MITT POPULATION WITH LOCF
TABLE 14.2.4.1.2	PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE) – STAGE 2	MITT POPULATION WITH LOCF
TABLE 14.2.4.1.3	**PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE) – COMBINED STAGE 1 AND STAGE 2**	**MITT POPULATION WITH LOCF**
TABLE 14.2.4.2.1	PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE) – STAGE 1	MITT2 POPULATION WITH LOCF
TABLE 14.2.4.2.2	PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE) – STAGE 2	MITT2 POPULATION WITH LOCF
TABLE 14.2.4.2.3	PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE) – COMBINED STAGE 1 AND STAGE 2	MITT2 POPULATION WITH LOCF
TABLE 14.2.4.3.1	PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE) – STAGE 1	PP POPULATION WITH LOCF
TABLE 14.2.4.3.2	PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE) – STAGE 2	PP POPULATION WITH LOCF
TABLE 14.2.4.3.3	PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE) – COMBINED STAGE 1 AND STAGE 2	PP POPULATION WITH LOCF
TABLE 14.2.4.4.1	PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE) – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.4.4.2	PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE) – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.4.4.3	PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE) - COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.4.5.1	PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE) – STAGE 1	MITT POPULATION WITH MCMC
TABLE 14.2.4.5.2	PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE) – STAGE 2	MITT POPULATION WITH MCMC
TABLE 14.2.4.5.3	PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE) – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH MCMC
TABLE 14.2.5.1.1	PRE-CAE® TOTAL OSDI© SCORE – STAGE 1	MITT POPULATION WITH LOCF
TABLE 14.2.5.1.2	PRE-CAE® TOTAL OSDI© SCORE – STAGE 2	MITT POPULATION WITH LOCF
TABLE 14.2.5.1.3	**PRE-CAE® TOTAL OSDI© SCORE – COMBINED STAGE 1 AND STAGE 2**	**MITT POPULATION WITH LOCF**
TABLE 14.2.5.2.1	PRE-CAE® TOTAL OSDI© SCORE – STAGE 1	MITT2 POPULATION WITH LOCF
TABLE 14.2.5.2.2	PRE-CAE® TOTAL OSDI© SCORE – STAGE 2	MITT2 POPULATION WITH LOCF
TABLE 14.2.5.2.3	PRE-CAE® TOTAL OSDI© SCORE – COMBINED STAGE 1 AND STAGE 2	MITT2 POPULATION WITH LOCF
TABLE 14.2.5.3.1	PRE-CAE® TOTAL OSDI© SCORE – STAGE 1	PP POPULATION WITH LOCF
TABLE 14.2.5.3.2	PRE-CAE® TOTAL OSDI© SCORE – STAGE 2	PP POPULATION WITH LOCF
TABLE 14.2.5.3.3	PRE-CAE® TOTAL OSDI© SCORE – COMBINED STAGE 1 AND STAGE 2	PP POPULATION WITH LOCF
TABLE 14.2.5.4.1	PRE-CAE® TOTAL OSDI© SCORE – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.5.4.2	PRE-CAE® TOTAL OSDI© SCORE – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY

Table Number	Title	Population
TABLE 14.2.5.4.3	PRE-CAE® TOTAL OSDI© SCORE – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.5.5.1	PRE-CAE® TOTAL OSDI© SCORE – STAGE 1	MITT POPULATION WITH MCMC
TABLE 14.2.5.5.2	PRE-CAE® TOTAL OSDI© SCORE – STAGE 2	MITT POPULATION WITH MCMC
TABLE 14.2.5.5.3	PRE-CAE® TOTAL OSDI© SCORE – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH MCMC
TABLE 14.2.6.1.1	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE) – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.6.1.2	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE) – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.6.1.3	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE) – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.6.2.1	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE) BY SUBGROUP – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.6.2.2	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE) BY SUBGROUP – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.6.2.3	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE) BY SUBGROUP – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.6.3.1	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE) BY BASELINE MEDIAN – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.6.3.2	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE) BY BASELINE MEDIAN – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.6.3.3	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE) BY BASELINE MEDIAN – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.7.1.1	FLUORESCEIN CORNEAL STAINING (OXFORD SCALE) – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.7.1.2	FLUORESCEIN CORNEAL STAINING (OXFORD SCALE) – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.7.1.3	FLUORESCEIN CORNEAL STAINING (OXFORD SCALE) – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.7.2.1	FLUORESCEIN CORNEAL STAINING (OXFORD SCALE) BY SUBGROUP – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.7.2.2	FLUORESCEIN CORNEAL STAINING (OXFORD SCALE) BY SUBGROUP – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.7.2.3	FLUORESCEIN CORNEAL STAINING (OXFORD SCALE) BY SUBGROUP – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.7.3.1	FLUORESCEIN CORNEAL STAINING (OXFORD SCALE) BY BASELINE MEDIAN – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.7.3.2	FLUORESCEIN CORNEAL STAINING (OXFORD SCALE) BY BASELINE MEDIAN – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.7.3.3	FLUORESCEIN CORNEAL STAINING (OXFORD SCALE) BY BASELINE MEDIAN – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.8.1.1	VISUAL ANALOG SCALE – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.8.1.2	VISUAL ANALOG SCALE – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY

Table Number	Title	Population
TABLE 14.2.8.1.3	VISUAL ANALOG SCALE – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.8.2.1	VISUAL ANALOG SCALE BY SUBGROUP – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.8.2.2	VISUAL ANALOG SCALE BY SUBGROUP – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.8.2.3	VISUAL ANALOG SCALE BY SUBGROUP – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.8.3.1	VISUAL ANALOG SCALE BY BASELINE MEDIAN – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.8.3.2	VISUAL ANALOG SCALE BY BASELINE MEDIAN – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.8.3.3	VISUAL ANALOG SCALE BY BASELINE MEDIAN – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.8.4.1	VISUAL ANALOG SCALE BY TIME TO CAE QUALIFICATION – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.8.4.2	VISUAL ANALOG SCALE BY TIME TO CAE QUALIFICATION – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.8.4.3	VISUAL ANALOG SCALE BY TIME TO CAE QUALIFICATION – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.9.1.1	OCULAR SURFACE DISEASE INDEX (OSDI) – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.9.1.2	OCULAR SURFACE DISEASE INDEX (OSDI) – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.9.1.3	OCULAR SURFACE DISEASE INDEX (OSDI) – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.9.2.1	OCULAR SURFACE DISEASE INDEX (OSDI) BY SUBGROUP – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.9.2.2	OCULAR SURFACE DISEASE INDEX (OSDI) BY SUBGROUP – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.9.2.3	OCULAR SURFACE DISEASE INDEX (OSDI) BY SUBGROUP – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.9.3.1	OCULAR SURFACE DISEASE INDEX (OSDI) BY BASELINE MEDIAN – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.9.3.2	OCULAR SURFACE DISEASE INDEX (OSDI) BY BASELINE MEDIAN – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.9.3.3	OCULAR SURFACE DISEASE INDEX (OSDI) BY BASELINE MEDIAN – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.9.4.1	OCULAR SURFACE DISEASE INDEX (OSDI) BY TIME TO CAE QUALIFICATION – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.9.4.2	OCULAR SURFACE DISEASE INDEX (OSDI) BY TIME TO CAE QUALIFICATION – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.9.4.3	OCULAR SURFACE DISEASE INDEX (OSDI) BY TIME TO CAE QUALIFICATION – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.10.1.1	UNANESTHETIZED SCHIRMER'S TEST (MM) – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.10.1.2	UNANESTHETIZED SCHIRMER'S TEST (MM) – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY

Table Number	Title	Population
TABLE 14.2.10.1.3	UNANESTHETIZED SCHIRMER'S TEST (MM) – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.10.2.1	UNANESTHETIZED SCHIRMER'S TEST (MM) STRATIFIED BY BASELINE MEDIAN – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.10.2.2	UNANESTHETIZED SCHIRMER'S TEST (MM) STRATIFIED BY BASELINE MEDIAN – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.10.2.3	UNANESTHETIZED SCHIRMER'S TEST (MM) STRATIFIED BY BASELINE MEDIAN – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.11.1.1	TEAR FILM BREAK-UP TIME (TFBUT) – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.11.1.2	TEAR FILM BREAK-UP TIME (TFBUT) – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.11.1.3	TEAR FILM BREAK-UP TIME (TFBUT) – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.11.2.1	TEAR FILM BREAK-UP TIME (TFBUT) STRATIFIED BY BASELINE MEDIAN – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.11.2.2	TEAR FILM BREAK-UP TIME (TFBUT) STRATIFIED BY BASELINE MEDIAN – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.11.2.3	TEAR FILM BREAK-UP TIME (TFBUT) STRATIFIED BY BASELINE MEDIAN – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.12.1.1	OCULUS KERATOGRAPH – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.12.1.2	OCULUS KERATOGRAPH – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.12.1.3	OCULUS KERATOGRAPH – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.12.2.1	OCULUS KERATOGRAPH STRATIFIED BY BASELINE MEDIAN – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.12.2.2	OCULUS KERATOGRAPH STRATIFIED BY BASELINE MEDIAN – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.12.2.3	OCULUS KERATOGRAPH STRATIFIED BY BASELINE MEDIAN – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.13.1.1	ORA CALIBRA® CONJUNCTIVAL REDNESS SCALE – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.13.1.2	ORA CALIBRA® CONJUNCTIVAL REDNESS SCALE – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.13.1.3	ORA CALIBRA® CONJUNCTIVAL REDNESS SCALE – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.13.2.1	ORA CALIBRA® CONJUNCTIVAL REDNESS SCALE STRATIFIED BY BASELINE MEDIAN – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.13.2.2	ORA CALIBRA® CONJUNCTIVAL REDNESS SCALE STRATIFIED BY BASELINE MEDIAN – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.13.2.3	ORA CALIBRA® CONJUNCTIVAL REDNESS SCALE STRATIFIED BY BASELINE MEDIAN – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.14.1.1	LISSAMINE GREEN CONJUNCTIVAL STAINING (OXFORD SCALE) – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.14.1.2	LISSAMINE GREEN CONJUNCTIVAL STAINING (OXFORD SCALE) – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY

Table Number	Title	Population
TABLE 14.2.14.1.3	LISSAMINE GREEN CONJUNCTIVAL STAINING (OXFORD SCALE) – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.14.2.1	LISSAMINE GREEN CONJUNCTIVAL STAINING (OXFORD SCALE) STRATIFIED BY BASELINE MEDIAN – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.14.2.2	LISSAMINE GREEN CONJUNCTIVAL STAINING (OXFORD SCALE) STRATIFIED BY BASELINE MEDIAN – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.14.2.3	LISSAMINE GREEN CONJUNCTIVAL STAINING (OXFORD SCALE) STRATIFIED BY BASELINE MEDIAN – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.15.1.1	ORA CALIBRA® OCULAR DISCOMFORT SCALE – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.15.1.2	ORA CALIBRA® OCULAR DISCOMFORT SCALE – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.15.1.3	ORA CALIBRA® OCULAR DISCOMFORT SCALE – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.15.2.1	ORA CALIBRA® OCULAR DISCOMFORT SCALE STRATIFIED BY BASELINE MEDIAN – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.15.2.2	ORA CALIBRA® OCULAR DISCOMFORT SCALE STRATIFIED BY BASELINE MEDIAN – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.15.2.3	ORA CALIBRA® OCULAR DISCOMFORT SCALE STRATIFIED BY BASELINE MEDIAN – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.15.3.1	ORA CALIBRA® OCULAR DISCOMFORT SCALE STRATIFIED BY TIME TO CAE QUALIFICATION – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.15.3.2	ORA CALIBRA® OCULAR DISCOMFORT SCALE STRATIFIED BY TIME TO CAE QUALIFICATION – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.15.3.3	ORA CALIBRA® OCULAR DISCOMFORT SCALE STRATIFIED BY TIME TO CAE QUALIFICATION – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.16.1.1	ORA CALIBRA® OCULAR DISCOMFORT SCALE (DURING CAE®) – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.16.1.2	ORA CALIBRA® OCULAR DISCOMFORT SCALE (DURING CAE®) – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.16.1.3	ORA CALIBRA® OCULAR DISCOMFORT SCALE (DURING CAE®) – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.16.2.1	ORA CALIBRA® OCULAR DISCOMFORT SCALE (DURING CAE®) STRATIFIED BY BASELINE MEDIAN – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.16.2.2	ORA CALIBRA® OCULAR DISCOMFORT SCALE (DURING CAE®) STRATIFIED BY BASELINE MEDIAN – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.16.2.3	ORA CALIBRA® OCULAR DISCOMFORT SCALE (DURING CAE®) STRATIFIED BY BASELINE MEDIAN – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.16.3.1	ORA CALIBRA® OCULAR DISCOMFORT SCALE (DURING CAE®) STRATIFIED BY TIME TO CAE QUALIFICATION – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.16.3.2	ORA CALIBRA® OCULAR DISCOMFORT SCALE (DURING CAE®) STRATIFIED BY TIME TO CAE QUALIFICATION – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.16.3.3	ORA CALIBRA® OCULAR DISCOMFORT SCALE (DURING CAE®) STRATIFIED BY TIME TO CAE QUALIFICATION – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY

Table Number	Title	Population
TABLE 14.2.17.1.1	ORA CALIBRA® OCULAR DISCOMFORT AND 4-SYMPTOM QUESTIONNAIRE – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.17.1.2	ORA CALIBRA® OCULAR DISCOMFORT AND 4-SYMPTOM QUESTIONNAIRE – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.17.1.3	ORA CALIBRA® OCULAR DISCOMFORT AND 4-SYMPTOM QUESTIONNAIRE – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.17.2.1	ORA CALIBRA® OCULAR DISCOMFORT AND 4-SYMPTOM QUESTIONNAIRE STRATIFIED BY BASELINE MEDIAN – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.17.2.2	ORA CALIBRA® OCULAR DISCOMFORT AND 4-SYMPTOM QUESTIONNAIRE STRATIFIED BY BASELINE MEDIAN – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.17.2.3	ORA CALIBRA® OCULAR DISCOMFORT AND 4-SYMPTOM QUESTIONNAIRE STRATIFIED BY BASELINE MEDIAN – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.17.3.1	ORA CALIBRA® OCULAR DISCOMFORT AND 4-SYMPTOM QUESTIONNAIRE STRATIFIED BY TIME TO CAE QUALIFICATION – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.17.3.2	ORA CALIBRA® OCULAR DISCOMFORT AND 4-SYMPTOM QUESTIONNAIRE STRATIFIED BY TIME TO CAE QUALIFICATION – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.17.3.3	ORA CALIBRA® OCULAR DISCOMFORT AND 4-SYMPTOM QUESTIONNAIRE STRATIFIED BY TIME TO CAE QUALIFICATION – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.18.1.1	SYMPTOM ASSESSMENT IN DRY EYE (SANDE) – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.18.1.2	SYMPTOM ASSESSMENT IN DRY EYE (SANDE) – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.18.1.3	SYMPTOM ASSESSMENT IN DRY EYE (SANDE) – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.18.2.1	SYMPTOM ASSESSMENT IN DRY EYE (SANDE) STRATIFIED BY BASELINE MEDIAN – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.18.2.2	SYMPTOM ASSESSMENT IN DRY EYE (SANDE) STRATIFIED BY BASELINE MEDIAN – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.18.2.3	SYMPTOM ASSESSMENT IN DRY EYE (SANDE) STRATIFIED BY BASELINE MEDIAN – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.18.3.1	SYMPTOM ASSESSMENT IN DRY EYE (SANDE) STRATIFIED BY TIME TO CAE QUALIFICATION – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.18.3.2	SYMPTOM ASSESSMENT IN DRY EYE (SANDE) STRATIFIED BY TIME TO CAE QUALIFICATION – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.18.3.3	SYMPTOM ASSESSMENT IN DRY EYE (SANDE) STRATIFIED BY TIME TO CAE QUALIFICATION – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.19.1.1	RESPONDER ANALYSIS – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.19.1.2	RESPONDER ANALYSIS – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.19.1.3	RESPONDER ANALYSIS – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY

Table Number	Title	Population
TABLE 14.2.20.1.1	RESPONDER SHIFT FROM BASELINE – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.20.1.2	RESPONDER SHIFT FROM BASELINE – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.20.1.3	RESPONDER SHIFT FROM BASELINE – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.21.1.1	P-VALUE SUMMARY – STAGE 1	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.21.1.2	P-VALUE SUMMARY – STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.2.21.1.3	P-VALUE SUMMARY – COMBINED STAGE 1 AND STAGE 2	MITT POPULATION WITH OBSERVED DATA ONLY
TABLE 14.3.1.1.1	ADVERSE EVENT SUMMARY – STAGE 1	SAFETY POPULATION
TABLE 14.3.1.1.2	ADVERSE EVENT SUMMARY – STAGE 2	SAFETY POPULATION
TABLE 14.3.1.1.3	**ADVERSE EVENT SUMMARY – COMBINED STAGE 1 AND STAGE 2**	**SAFETY POPULATION**
TABLE 14.3.1.2.1	ALL OCULAR ADVERSE EVENTS	SAFETY POPULATION
TABLE 14.3.1.2.2	ALL OCULAR ADVERSE EVENTS – STAGE 2	SAFETY POPULATION
TABLE 14.3.1.2.3	ALL OCULAR ADVERSE EVENTS – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.1.3.1	ALL NON-OCULAR ADVERSE EVENTS – STAGE 1	SAFETY POPULATION
TABLE 14.3.1.3.2	ALL NON-OCULAR ADVERSE EVENTS – STAGE 2	SAFETY POPULATION
TABLE 14.3.1.3.3	ALL NON-OCULAR ADVERSE EVENTS – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.1.4.1	ALL OCULAR TREATMENT-EMERGENT ADVERSE EVENTS – STAGE 1	SAFETY POPULATION
TABLE 14.3.1.4.2	ALL OCULAR TREATMENT-EMERGENT ADVERSE EVENTS – STAGE 2	SAFETY POPULATION
TABLE 14.3.1.4.3	**ALL OCULAR TREATMENT-EMERGENT ADVERSE EVENTS – COMBINED STAGE 1 AND STAGE 2**	**SAFETY POPULATION**
TABLE 14.3.1.5.1	ALL NON-OCULAR TREATMENT-EMERGENT ADVERSE EVENTS – STAGE 1	SAFETY POPULATION
TABLE 14.3.1.5.2	ALL NON-OCULAR TREATMENT-EMERGENT ADVERSE EVENTS – STAGE 2	SAFETY POPULATION
TABLE 14.3.1.5.3	ALL NON-OCULAR TREATMENT-EMERGENT ADVERSE EVENTS – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.1.6.1	ALL OCULAR TREATMENT-RELATED TREATMENT-EMERGENT ADVERSE EVENTS – STAGE 1	SAFETY POPULATION
TABLE 14.3.1.6.2	ALL OCULAR TREATMENT-RELATED TREATMENT-EMERGENT ADVERSE EVENTS – STAGE 2	SAFETY POPULATION
TABLE 14.3.1.6.3	ALL OCULAR TREATMENT-RELATED TREATMENT-EMERGENT ADVERSE EVENTS – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.1.7.1	ALL NON-OCULAR TREATMENT-RELATED TREATMENT-EMERGENT ADVERSE EVENTS – STAGE 1	SAFETY POPULATION
TABLE 14.3.1.7.2	ALL NON-OCULAR TREATMENT-RELATED TREATMENT-EMERGENT ADVERSE EVENTS – STAGE 2	SAFETY POPULATION

Table Number	Title	Population
TABLE 14.3.1.7.3	ALL NON-OCULAR TREATMENT-RELATED TREATMENT-EMERGENT ADVERSE EVENTS – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.1.8.1	ALL SERIOUS ADVERSE EVENTS – STAGE 1	SAFETY POPULATION
TABLE 14.3.1.8.2	ALL SERIOUS ADVERSE EVENTS – STAGE 2	SAFETY POPULATION
TABLE 14.3.1.8.3	**ALL SERIOUS ADVERSE EVENTS – COMBINED STAGE 1 AND STAGE 2**	**SAFETY POPULATION**
TABLE 14.3.1.9.1	ALL OCULAR TREATMENT-EMERGENT ADVERSE EVENTS BY MAXIMAL SEVERITY – STAGE 1	SAFETY POPULATION
TABLE 14.3.1.9.2	ALL OCULAR TREATMENT-EMERGENT ADVERSE EVENTS BY MAXIMAL SEVERITY – STAGE 2	SAFETY POPULATION
TABLE 14.3.1.9.3	ALL OCULAR TREATMENT-EMERGENT ADVERSE EVENTS BY MAXIMAL SEVERITY – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.1.10.1	ALL NON-OCULAR TREATMENT-EMERGENT ADVERSE EVENTS BY MAXIMAL SEVERITY – STAGE 1	SAFETY POPULATION
TABLE 14.3.1.10.2	ALL NON-OCULAR TREATMENT-EMERGENT ADVERSE EVENTS BY MAXIMAL SEVERITY – STAGE 2	SAFETY POPULATION
TABLE 14.3.1.10.3	ALL NON-OCULAR TREATMENT-EMERGENT ADVERSE EVENTS BY MAXIMAL SEVERITY – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.1.11.1	ALL OCULAR TREATMENT-EMERGENT ADVERSE EVENTS BY STUDY DAY OF ONSET – STAGE 1	SAFETY POPULATION
TABLE 14.3.1.11.2	ALL OCULAR TREATMENT-EMERGENT ADVERSE EVENTS BY STUDY DAY OF ONSET – STAGE 2	SAFETY POPULATION
TABLE 14.3.11.3	ALL OCULAR TREATMENT-EMERGENT ADVERSE EVENTS BY STUDY DAY OF ONSET – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.1.12.1	ALL NON-OCULAR TREATMENT-EMERGENT ADVERSE EVENTS BY STUDY DAY OF ONSET – STAGE 2	SAFETY POPULATION
TABLE 14.3.1.12.2	ALL NON-OCULAR TREATMENT-EMERGENT ADVERSE EVENTS BY STUDY DAY OF ONSET – STAGE 2	SAFETY POPULATION
TABLE 14.3.1.12.3	ALL NON-OCULAR TREATMENT-EMERGENT ADVERSE EVENTS BY STUDY DAY OF ONSET – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.2.1	ORA CALIBRA® DROP COMFORT SCALE – STAGE 1	SAFETY POPULATION
TABLE 14.3.2.2	ORA CALIBRA® DROP COMFORT SCALE – STAGE 2	SAFETY POPULATION
TABLE 14.3.2.3	ORA CALIBRA® DROP COMFORT SCALE – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.3.1	ORA CALIBRA® DROP COMFORT QUESTIONNAIRE – STAGE 1	SAFETY POPULATION
TABLE 14.3.3.2	ORA CALIBRA® DROP COMFORT QUESTIONNAIRE – STAGE 2	SAFETY POPULATION
TABLE 14.3.3.3	ORA CALIBRA® DROP COMFORT QUESTIONNAIRE – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.4.1	BEST-CORRECTED VISUAL ACUITY (BCVA; LOGMAR) – STAGE 1	SAFETY POPULATION
TABLE 14.3.4.2	BEST-CORRECTED VISUAL ACUITY (BCVA; LOGMAR) – STAGE 2	SAFETY POPULATION
TABLE 14.3.4.3	BEST-CORRECTED VISUAL ACUITY (BCVA; LOGMAR) – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.5.1.1	SLIT-LAMP BIOMICROSCOPY – STAGE 1	SAFETY POPULATION
TABLE 14.3.5.1.2	SLIT-LAMP BIOMICROSCOPY – STAGE 2	SAFETY POPULATION
TABLE 14.3.5.1.3	SLIT-LAMP BIOMICROSCOPY – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION

Table Number	Title	Population
TABLE 14.3.5.2.1	SHIFT IN SLIT-LAMP BIOMICROSCOPY – STAGE 1	SAFETY POPULATION
TABLE 14.3.5.2.2	SHIFT IN SLIT-LAMP BIOMICROSCOPY – STAGE 2	SAFETY POPULATION
TABLE 14.3.5.2.3	SHIFT IN SLIT-LAMP BIOMICROSCOPY – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.6.1	INTRAOCULAR PRESSURE (IOP; MMHG) – STAGE 1	SAFETY POPULATION
TABLE 14.3.6.2	INTRAOCULAR PRESSURE (IOP; MMHG) – STAGE 2	SAFETY POPULATION
TABLE 14.3.6.3	INTRAOCULAR PRESSURE (IOP; MMHG) – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.7.1.1	OPHTHALMOSCOPY – STAGE 1	SAFETY POPULATION
TABLE 14.3.7.1.2	OPHTHALMOSCOPY – STAGE 2	SAFETY POPULATION
TABLE 14.3.7.1.3	OPHTHALMOSCOPY – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.7.2.1	SHIFT IN OPHTHALMOSCOPY – STAGE 1	SAFETY POPULATION
TABLE 14.3.7.2.2	SHIFT IN OPHTHALMOSCOPY – STAGE 2	SAFETY POPULATION
TABLE 14.3.7.2.3	SHIFT IN OPHTHALMOSCOPY – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.8.1	VITAL SIGNS – STAGE 1	SAFETY POPULATION
TABLE 14.3.8.2	VITAL SIGNS – STAGE 2	SAFETY POPULATION
TABLE 14.3.8.3	VITAL SIGNS – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.9.1	LABORATORY TESTS – STAGE 1	SAFETY POPULATION
TABLE 14.3.9.2	LABORATORY TESTS – STAGE 2	SAFETY POPULATION
TABLE 14.3.9.3	LABORATORY TESTS – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.10.1	COMPLIANCE WITH STUDY DRUG – STAGE 1	SAFETY POPULATION
TABLE 14.3.10.2	COMPLIANCE WITH STUDY DRUG – STAGE 2	SAFETY POPULATION
TABLE 14.3.10.3	COMPLIANCE WITH STUDY DRUG – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION
TABLE 14.3.11.1	EXPOSURE TO STUDY DRUG – STAGE 1	SAFETY POPULATION
TABLE 14.3.11.2	EXPOSURE TO STUDY DRUG – STAGE 2	SAFETY POPULATION
TABLE 14.3.11.3	EXPOSURE TO STUDY DRUG – COMBINED STAGE 1 AND STAGE 2	SAFETY POPULATION

21. Listings

Listing Number	Title
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LISTING 16.1.7.2	RANDOMIZATION – STAGE 2
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LISTING 16.2.1.2	SUBJECT DISPOSITION – STAGE 2
LISTING 16.2.2.1	PROTOCOL DEVIATIONS – STAGE 1
LISTING 16.2.2.2	PROTOCOL DEVIATIONS – STAGE 2
LISTING 16.2.3.1	STUDY POPULATION INCLUSION – STAGE 1
LISTING 16.2.3.2	STUDY POPULATION INCLUSION – STAGE 2
LISTING 16.2.4.1.1	DEMOGRAPHICS – STAGE 1
LISTING 16.2.4.1.2	DEMOGRAPHICS – STAGE 2
LISTING 16.2.4.2.1	OCULAR MEDICAL HISTORY – STAGE 1

Listing Number	Title
LISTING 16.2.4.2.2	OCULAR MEDICAL HISTORY – STAGE 2
LISTING 16.2.4.3.1	NON-OCULAR MEDICAL HISTORY – STAGE 1
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LISTING 16.2.5.1.1	PRIOR AND CONCOMITANT OCULAR MEDICATIONS – STAGE 1
LISTING 16.2.5.1.2	PRIOR AND CONCOMITANT OCULAR MEDICATIONS – STAGE 2
LISTING 16.2.5.2.1	PRIOR AND CONCOMITANT NON-OCULAR MEDICATIONS – STAGE 1
LISTING 16.2.5.2.1	PRIOR AND CONCOMITANT NON-OCULAR MEDICATIONS – STAGE 2
LISTING 16.2.5.3.1	IN-OFFICE STUDY MEDICATION INSTILLATION – STAGE 1
LISTING 16.2.5.3.2	IN-OFFICE STUDY MEDICATION INSTILLATION – STAGE 2
LISTING 16.2.5.4.1	STUDY DRUG EXPOSURE AND DOSING COMPLIANCE – STAGE 1
LISTING 16.2.5.4.2	STUDY DRUG EXPOSURE AND DOSING COMPLIANCE – STAGE 2
LISTING 16.2.5.5.1	STUDY DRUG ACCOUNTABILITY – STAGE 1
LISTING 16.2.5.5.2	STUDY DRUG ACCOUNTABILITY – STAGE 2
LISTING 16.2.6.1.1	CORNEAL AND CONJUNCTIVAL FLUORESCEIN STAINING (ORA CALIBRA® AND OXFORD SCALES) – STAGE 1
LISTING 16.2.6.1.2	CORNEAL AND CONJUNCTIVAL FLUORESCEIN STAINING (ORA CALIBRA® AND OXFORD SCALES) – STAGE 2
LISTING 16.2.6.2.1	VISUAL ANALOGUE SCALE (VAS) – STAGE 1
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LISTING 16.2.6.3.1	OCULAR SURFACE DISEASE INDEX (OSDI; PRE-CAE) – STAGE 1
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LISTING 16.2.6.4.1	UNANESTHETIZED SCHIRMER'S TEST (PRE-CAE) – STAGE 1
LISTING 16.2.6.4.2	UNANESTHETIZED SCHIRMER'S TEST (PRE-CAE) – STAGE 2
LISTING 16.2.6.5.1	TEAR FILM BREAK-UP TIME (TFBUT) – STAGE 1
LISTING 16.2.6.5.2	TEAR FILM BREAK-UP TIME (TFBUT) – STAGE 2
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LISTING 16.2.6.6.1	ORA CALIBRA® CONJUNCTIVAL REDNESS SCALE FOR BULBAR CONJUNCTIVAL HYPEREMIA – STAGE 1
LISTING 16.2.6.6.2	ORA CALIBRA® CONJUNCTIVAL REDNESS SCALE FOR BULBAR CONJUNCTIVAL HYPEREMIA – STAGE 2
LISTING 16.2.6.7.1	LISSAMINE GREEN CONJUNCTIVAL STAINING (OXFORD SCALE) – STAGE 1
LISTING 16.2.6.7.2	LISSAMINE GREEN CONJUNCTIVAL STAINING (OXFORD SCALE) – STAGE 2
LISTING 16.2.6.8.1	ORA CALIBRA® OCULAR DISCOMFORT SCALE PRE-, POST-, AND NON-CAE – STAGE 1
LISTING 16.2.6.8.2	ORA CALIBRA® OCULAR DISCOMFORT SCALE PRE-, POST-, AND NON-CAE – STAGE 2
LISTING 16.2.6.9.1	ORA CALIBRA® OCULAR DISCOMFORT SCALE DURING CAE EXPOSURE – STAGE 1
LISTING 16.2.6.9.2	ORA CALIBRA® OCULAR DISCOMFORT SCALE DURING CAE EXPOSURE – STAGE 2
LISTING 16.2.6.10.1	ORA CALIBRA® OCULAR DISCOMFORT AND 4-SYMPTOM QUESTIONNAIRE – STAGE 1
LISTING 16.2.6.10.2	ORA CALIBRA® OCULAR DISCOMFORT AND 4-SYMPTOM QUESTIONNAIRE – STAGE 2
LISTING 16.2.6.11.1	SYMPTOM ASSESSMENT IN DRY EYE (SANDE; PRE-CAE) – STAGE 1

Listing Number	Title
LISTING 16.2.6.11.2	SYMPTOM ASSESSMENT IN DRY EYE (SANDE; PRE-CAE) – STAGE 2
LISTING 16.2.6.12.1	TEAR COLLECTION (PRE-CAE) – STAGE 1
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LISTING 16.2.7.1.1.1	ALL ADVERSE EVENTS – STAGE 1
LISTING 16.2.7.1.1.2	ALL ADVERSE EVENTS – STAGE 2
LISTING 16.2.7.1.2.1	ADVERSE EVENTS LEADING TO TREATMENT DISCONTINUATION – STAGE 1
LISTING 16.2.7.1.2.2	ADVERSE EVENTS LEADING TO TREATMENT DISCONTINUATION – STAGE 2
LISTING 16.2.7.1.3.1	ADVERSE EVENTS LEADING TO DEATH – STAGE 1
LISTING 16.2.7.1.3.2	ADVERSE EVENTS LEADING TO DEATH – STAGE 2
LISTING 16.2.7.1.4.1	ALL SERIOUS ADVERSE EVENTS – STAGE 1
LISTING 16.2.7.1.4.2	ALL SERIOUS ADVERSE EVENTS – STAGE 2
LISTING 16.2.7.2.1	ORA CALIBRA® DROP COMFORT SCALE – STAGE 1
LISTING 16.2.7.2.2	ORA CALIBRA® DROP COMFORT SCALE – STAGE 2
LISTING 16.2.7.2.3	ORA CALIBRA® DROP COMFORT QUESTIONNAIRE 3 MINUTES POST-INSTALLATION – STAGE 1
LISTING 16.2.7.2.4	ORA CALIBRA® DROP COMFORT QUESTIONNAIRE 3 MINUTES POST-INSTALLATION – STAGE 2
LISTING 16.2.7.3.1.1	BEST-CORRECTED VISUAL ACUITY (BCVA; LOGMAR) (PRE-CAE) – STAGE 1
LISTING 16.2.7.3.1.2	BEST-CORRECTED VISUAL ACUITY (BCVA; LOGMAR) (PRE-CAE) – STAGE 2
LISTING 16.2.7.3.2.1	SLIT LAMP BIOMICROSCOPY – STAGE 1
LISTING 16.2.7.3.2.2	SLIT LAMP BIOMICROSCOPY – STAGE 2
LISTING 16.2.7.3.3.1	OPHTHALMOSCOPY (POST-CAE) – STAGE 1
LISTING 16.2.7.3.3.2	OPHTHALMOSCOPY (POST-CAE) – STAGE 2
LISTING 16.2.7.3.4.1	INTRAOCULAR PRESSURE (IOP; POST-CAE) – STAGE 1
LISTING 16.2.7.3.4.2	INTRAOCULAR PRESSURE (IOP; POST-CAE) – STAGE 2
LISTING 16.2.8.1.1	BLOOD CHEMISTRY – STAGE 1
LISTING 16.2.8.1.2	BLOOD CHEMISTRY – STAGE 2
LISTING 16.2.8.2.1	HEMATOLOGY – STAGE 1
LISTING 16.2.8.2.2	HEMATOLOGY – STAGE 2
LISTING 16.2.8.3.1	URINALYSIS – STAGE 1
LISTING 16.2.8.3.2	URINALYSIS – STAGE 2
LISTING 16.2.8.4	PHARMACOKINETICS SAMPLES
LISTING 16.2.9.1.1	VITAL SIGNS (PRE-CAE) – STAGE 1
LISTING 16.2.9.1.2	VITAL SIGNS (PRE-CAE) – STAGE 2
LISTING 16.2.9.2.1	CHILDBEARING POTENTIAL AND URINE PREGNANCY TEST – STAGE 1
LISTING 16.2.9.2.2	CHILDBEARING POTENTIAL AND URINE PREGNANCY TEST – STAGE 2

22. Figures

Figure Number	Title	Population
FIGURE 14.2.1.1	PRE-CAE® INFERIOR FLUORESCEIN STAINING (ORA CALIBRA® SCALE) CHANGE FROM BASELINE – STAGE 1	MITT POPULATION WITH LOCF

Figure Number	Title	Population
FIGURE 14.2.1.2	PRE-CAE® INFERIOR FLUORESCEIN STAINING (ORA CALIBRA® SCALE) CHANGE FROM BASELINE – STAGE 2	MITT POPULATION WITH LOCF
FIGURE 14.2.1.3	**PRE-CAE® INFERIOR FLUORESCEIN STAINING (ORA CALIBRA® SCALE) CHANGE FROM BASELINE – COMBINED STAGE 1 AND STAGE 2**	**MITT POPULATION WITH LOCF**
FIGURE 14.2.2.1	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) CHANGE FROM BASELINE – STAGE 1	MITT POPULATION WITH LOCF
FIGURE 14.2.2.2	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) CHANGE FROM BASELINE – STAGE 2	MITT POPULATION WITH LOCF
FIGURE 14.2.2.3	**PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (ORA CALIBRA® SCALE) CHANGE FROM BASELINE – COMBINED STAGE 1 AND STAGE 2**	**MITT POPULATION WITH LOCF**
FIGURE 14.2.3.1	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE) CHANGE FROM BASELINE – STAGE 1	MITT POPULATION WITH LOCF
FIGURE 14.2.3.2	PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE) CHANGE FROM BASELINE – STAGE 2	MITT POPULATION WITH LOCF
FIGURE 14.2.3.3	**PRE-CAE® TOTAL CORNEAL FLUORESCEIN STAINING (OXFORD SCALE) CHANGE FROM BASELINE – COMBINED STAGE 1 AND STAGE 2**	**MITT POPULATION WITH LOCF**
FIGURE 14.2.4.1	PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE) CHANGE FROM BASELINE – STAGE 1	MITT POPULATION WITH LOCF
FIGURE 14.2.4.2	PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE) CHANGE FROM BASELINE – STAGE 2	MITT POPULATION WITH LOCF
FIGURE 14.2.4.3	**PRE-CAE® EYE DRYNESS (VISUAL ANALOG SCALE) CHANGE FROM BASELINE – COMBINED STAGE 1 AND STAGE 2**	**MITT POPULATION WITH LOCF**
FIGURE 14.2.5.1	PRE-CAE® TOTAL OSDI© SCORE CHANGE FROM BASELINE – STAGE 1	MITT POPULATION WITH LOCF
FIGURE 14.2.5.2	PRE-CAE® TOTAL OSDI© SCORE CHANGE FROM BASELINE – STAGE 2	MITT POPULATION WITH LOCF
FIGURE 14.2.5.3	**PRE-CAE® TOTAL OSDI© SCORE CHANGE FROM BASELINE – COMBINED STAGE 1 AND STAGE 2**	**MITT POPULATION WITH LOCF**