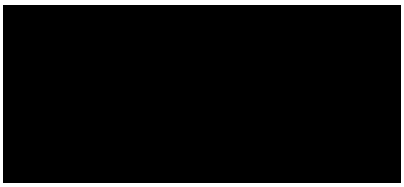

STATISTICAL ANALYSIS PLAN

PROTOCOL NUMBER: CPN-302

A Multicenter, Randomized, Double-Masked, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of APP13007 for the Treatment of Inflammation and Pain after Cataract Surgery, Including a Corneal Endothelial Cell Sub-study

Version No.	Final 1.1
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APPROVAL SIGNATURE PAGE

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SUMMARY OF CHANGES IN SAP AMENDMENT 1

- Clarified Study Day calculation corresponding to Surgery Day 0 and Screening Visit (Day -28 to Day -1) nomenclature in the protocol (Section 6.3.4)
- Revised the range of study days for the Analysis Window and rules for handling data when multiple efficacy assessments fall within the same analysis window for an Analysis Visit (Section 6.3.5)
- Clarified the LOCF approach to be used for the secondary efficacy endpoints in response to FDA's comments (dated November 3, 2021) on the final SAP v1.0 (Sections 6.4.2 and 6.4.3.1)
- Included three iris color categories in the subgroup of iris color (Section 6.4.7)
- Clarified missing data for "Observed-Case" sensitivity analysis of the primary endpoints (Section 10.1.3)
- Revised the data handling rule from using the LOCF approach to using observed data for the Additional Analysis (Section 10.1.4)
- Provided the definition of rescue medication use during the treatment period and clarified that only the first time of rescue medication use will be included in the analysis and summary when multiple rescue medications are used by a subject (Section 10.2.2.3)
- Added the categories of the number of doses received per subject and revised the categories of treatment duration (Section 11.1)
- Clarified only ocular adverse events will be summarized by relationship to both study drug and surgery, and then separately by relationship to surgery only (Section 11.2)
- Clarified the use of BCVA Base LogMar score (Section 11.3.2)

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LIST OF ABBREVIATIONS

Abbreviation	Definition
ACC	Anterior Chamber Cell
ACF	Anterior Chamber Flare
AE	Adverse Event
ANCOVA	Analyses of Covariance
ATC	Anatomical Therapeutic Chemical
BCVA	Best Corrected Visual Acuity
BID	Twice Daily
CI	Confidence Interval
CV	Coefficient of Variation
eCRF	Electronic Case Report Form
EOMS	End of Main Study
EOSS	End of Sub-Study
ETDRS	Early Treatment of Diabetic Retinopathy Study
IOP	Intraocular Pressure
ITT	Intent-to-Treat
LOCF	Last Observation Carried Forward
MedDRA	Medical Dictionary for Regulatory Activities
OD	Right Eye
OS	Left Eye
OU	Both Eyes
POD	Post-Operative Day
PP	Per-Protocol
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOC	System Organ Class
SUSAR	Serious and Unexpected Suspected Adverse Reaction
TEAE	Treatment-Emergent Adverse Event
WHO	World Health Organization

1. INTRODUCTION

This document is prepared in compliance with International Conference on Harmonization E9 and intended to provide details of statistical methodology and data handling rules to be used for the analyses of data from Protocol CPN-302 v1.2 (Amendment 1): A Multicenter, Randomized, Double-Masked, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of APP13007 for the Treatment of Inflammation and Pain after Cataract Surgery, Including a Corneal Endothelial Cell Sub-study. This Phase 3 study is being conducted in the United States.

2. STUDY OBJECTIVES AND ENDPOINTS

The study objectives and corresponding study endpoints are presented in Table 1 below:

Table 1: Study Objectives and Endpoints

Objectives	Endpoints
Primary Efficacy Objective The primary efficacy objective is to investigate the efficacy of APP13007 versus matching vehicle placebo for the treatment of inflammation and pain through post-operative day (POD) 15 after cataract surgery in the study eye.	Primary Efficacy Endpoints • The proportion of subjects with Anterior Chamber Cell (ACC) Count = 0 [ACC Grade = 0] at post-operative day 8 (POD8), maintained through POD15 • The proportion of subjects with Ocular Pain Grade = 0 at POD4, maintained through POD15
Secondary Efficacy Objective The secondary efficacy objective of this study is to investigate the effect of APP13007 versus matching vehicle placebo on markers of inflammation, ocular pain and visual acuity after cataract surgery in the study eye.	Secondary Efficacy Endpoints • Proportion of subjects with ACC count = 0 [ACC Grade = 0] at PODs 4, 8 and 15 • Proportion of subjects with Ocular Pain Grade = 0 at PODs 4, 8 and 15 • Proportion of subjects with Anterior chamber flare (ACF) Grade = 0 at POD8 maintained through POD15 • Proportion of subjects with ACF Grade = 0 at PODs 4, 8 and 15 • Mean change-from-baseline in ACC Grade at PODs 4, 8, and 15 • Mean change-from-baseline in Ocular Pain Grade at PODs 4, 8 and 15 • Mean change-from-baseline in ACF Grade on PODs 4, 8 and 15 • Number of subjects rescued on or prior to each visit and overall • Mean change-from-baseline in best corrected visual acuity by pinhole method using an Early Treatment Diabetic Retinopathy Study (ETDRS) chart at PODs 4, 8 and 15

Objectives	Endpoints

Safety Objective
The safety objective is to investigate the safety and tolerability of APP13007 versus matching vehicle placebo for the treatment of inflammation and pain after cataract surgery.
	Safety Endpoints
	• Adverse events (AEs)
	• Best corrected visual acuity by pinhole method using an ETDRS chart from baseline to each post-surgery visit
	• Slit-lamp biomicroscopy
	  o Change-from-baseline in ocular signs to each post-surgery visit
	• Dilated indirect ophthalmoscopy
	  o Change-from-baseline in ocular signs to Visit 6 (POD22)
	• Mean changes in corneal endothelial cell density, percent hexagonality and coefficient of variation from baseline (Visit 1/Screening) to Visit 7 (POD85) in the study eye in subjects in the Endothelial Cell Sub-study
	• Intraocular pressure (IOP) at each visit and change-from-baseline to Visit 6 (POD22) measured with a Goldmann applanation tonometer

3. STUDY DESIGN

3.1 Study Design Overview

This Phase 3 study will evaluate APP13007 [redacted] in comparison to the matching vehicle placebo in a randomized, parallel-group, double-masked fashion. Subjects will have routine uncomplicated cataract surgery on Day 0 of the study and will be assessed the next day (POD1) after the surgery for eligibility for randomization to study treatment. The study comprises the Main Study and the Endothelial Cell Sub-study. All randomized subjects (approximately 370) will participate in the Main Study. The Endothelial Cell Sub-study will comprise a subgroup of approximately 176 subjects at study sites qualified to perform corneal endothelial cell parameter assessments.

All eligible subjects at the qualified study sites for corneal endothelial cell assessments will be requested to participate in the Sub-study. If a subject is unable or unwilling to participate in the Sub-study, the Investigator has the option to enroll the subject in the Main Study only, after consulting with the Study Medical Monitor.

Subjects who experience postoperative inflammation on POD1 and who meet all other eligibility criteria will be randomized, at a 1:1 ratio, to one of two study treatments (either Treatment 1 or Treatment 2):

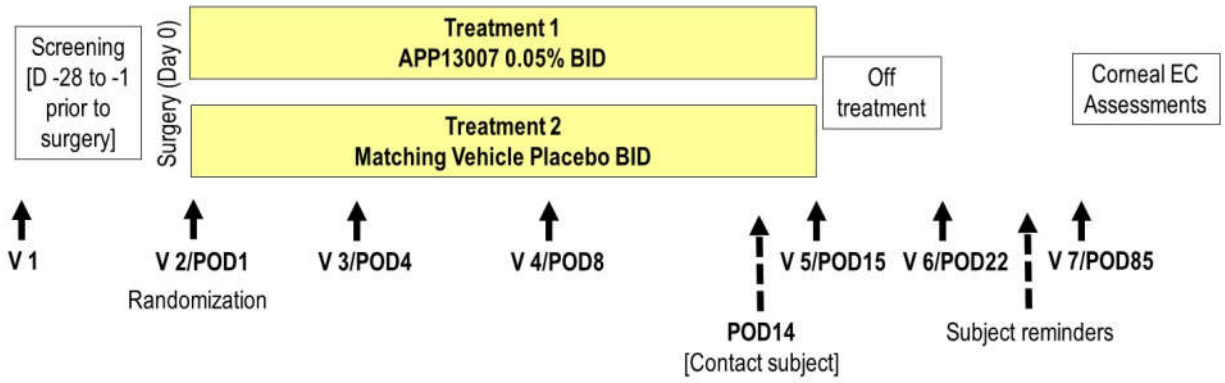
- Treatment 1: 1 drop APP13007 twice daily (BID) (morning and evening) for 14 days instilled to the operated study eye
- Treatment 2: 1 drop matching vehicle placebo BID (morning and evening) for 14 days instilled to the operated study eye

After randomization, the first dose of study drug will be administered in the clinic on POD1 so that the site personnel can ensure the subject is able to administer the study drug correctly. The second drop of the study drug on POD1 will be administered by the subject a minimum of 6 hours later. For all other days, the first dose will be instilled in the morning and the second dose instilled a minimum of 6 hours, but preferably 8 to 12 hours, later. The number of drop(s) instilled and the date/time of instillation of each dose will be recorded by the subject in the subject's dosing diary. The study drug will be dosed BID for 14 days.

Any subjects who have evidence of persistent or worsening inflammation as described in the protocol Section 9.4 may be rescued and placed on appropriate alternate therapy. The choice of rescue medication is at the Investigator's discretion. Rescued subjects will stop study drug and will not be withdrawn from the study. The rescued subjects will continue to be assessed at each subsequent visit, if possible, through completion of the Visit 6/POD22 assessments for the subjects in the Main study only or through completion of the Visit 7/POD85 assessments for the subjects in the Sub-study.

This study will include up to 7 scheduled clinic visits (including the surgery day) over a range of ~ 24 to ~ 51 days for the subjects in the Main Study who are not participating in the Endothelial Cell Sub-study, while subjects in the Endothelial Cell Sub-study will have up to 8 scheduled clinic visits (including the surgery day) over a range of ~ 87 to ~ 114 days (Figure 1). Subjects who are not participating in the Endothelial Cell sub-study will be discharged from the study after the assessments for Visit 6/POD22 have been performed. Subjects who are participating in the Endothelial Cell sub-study will be discharged from the study after the assessments for Visit 7/POD85 have been performed.

Figure 1: Study Schematic



3.2 Schedule of Events

All assessments including ocular assessments and safety assessments are outlined in Table 2.

Table 2: Schedule of Events

PROCEDURE/ASSESSMENTS [1]	Visit 1 Screening (Day -28 to -1)	Surgery [2] Day 0	Visit 2 POD1 [3]	Visit 3 POD4 (±1 Day)	Visit 4 POD8 (±1 Day)	Contact POD14	Visit 5 POD15 (+1 Day) [4]	Visit 6 POD22 (±2 Days) [5]	Reminders (~POD50 and ~POD78)	Visit 7 POD85 (±4 Days) [6]
ICF, Demography, Medical History	X									
Determine Eligibility, Review Inclusion/Exclusion Criteria	X		X							
Urine pregnancy test only for women of child-bearing potential			X				X			
Ocular Symptoms Assessment [7]	X		X	X	X		X	X		
ETDRS Visual Acuity	X		X	X	X		X	X		
Slit Lamp Biomicroscopy [8]	X		X	X	X		X	X		
Indirect Ophthalmoscopy (dilated)	X							X		
IOP (Goldmann applanation tonometry) [9]	X		X	X	X		X	X		
Corneal Endothelial Cell Parameters [10]	X							X		X
Randomization			X							
Dispense Study Drug			X							
Study Drug Dosing BID for 14 days (POD1 to POD14) [11]			X	X	X	X				
Dispense Diary Card (with instructions for completion)			X	X	X					
Contact Subject [12]						X			X	
Collect Study Drug							X			
Collect and Check Diary Cards for Accuracy and Compliance				X	X		X			
AEs [7] and Concomitant Medications [13]	X	X [14]	X	X	X	X [15]	X	X		X [15]

[1] Ophthalmic assessments will be performed in the study eye only at Visits 2-5 and Visit 7 and performed on both eyes at Visit 1 (Screening) and at Visit 6 (POD22) or at subject Early Termination/Withdrawal. In the Endothelial Cell Sub-study, corneal endothelial cell parameters are measured in both eyes at Screening and in the study eye only at Visit 6 (POD22) and Visit 7 (POD85).

[2] Surgery must occur between one to 28 days after Screening, preferably in the morning. If, due to unexpected events, surgery is postponed and would occur > 28 days past the Screening visit, contact the Study Medical Monitor to determine which, if any, of the screening procedures should be repeated. Subjects will be determined to be a suitable candidate for surgery during a pre-surgery medical assessment, where the routine medication list prescribed by the cataract surgeon should be reviewed to rule out prohibited medications (protocol Section 5.4.2).

[3] Visit 2 (POD1) should be scheduled between 18 to 34 hours following conclusion of surgery on Day 0. All assessments done on POD1 are done prior to Randomization to ensure eligibility. Note: Women-of-childbearing-potential are eligible for enrollment if they have a negative urine pregnancy test on POD1 prior to Randomization and they agree to abstinence from sexual activity or use of highly effective method of contraception from POD1 to Visit 6 (POD22).

[4] Visit 5 (POD15) occurs on the day after the subject completes the study drug administration for 14 days. Women-of-childbearing-potential should have a urine pregnancy test.

[5] Visit 6 (POD22) is the last visit for subjects participating in the Main Study only. Subjects who are withdrawn early should have the Visit 6 assessments and a urine pregnancy test, if applicable, performed before they are released from the study.

[6] Visit 7 (POD85) is the last visit for subjects participating in the Endothelial Cell Sub-study.

[7] Includes assessments of ocular pain and irritation. See protocol Section 8.0 for information on how to record AEs and how to determine attributability (relatedness) of AE to study procedures (including cataract surgery) or study drug.

[8] Ocular inflammation assessment using ACC count, anterior chamber flare grade, bulbar conjunctival injection, sclera - ciliary flush and corneal edema.

[9] IOP should (but not required) be assessed at each visit within ± 2 h of the IOP assessment time at Visit 1.

[10] Only performed in the subjects in the Endothelial Cell Sub-study at participating centers. The parameters are: endothelial cell density (cells/mm^2), percent hexagonality and coefficient of variation. Performed in both eyes at the Screening visit and in the study eye at Visit 6 (POD22) and Visit 7 (POD85).

[11] The first dose of study drug should be instilled into the study eye at the clinic visit under supervision of clinic staff. The second dose on POD1 can be administered at home. Subjects who are rescued will not continue to instill study drug or receive further diary cards but will remain in the study to complete the procedures/assessments through Visit 6 (POD22) (Main Study) or Visit 7 (Endothelial Cell Sub-study).

[12] The site must contact the subject via the subject's preferred method on POD14 to remind him/her not to instill study drug on POD15 and to bring the bottle of study drug and the dosing diary back to the site at the POD15 visit. In addition, the subjects in the Endothelial Cell Sub-study will be sent US mail/email/voicemail/text message reminders on ~POD50 and ~POD78 to return for Visit 7 (POD85).

[13] Concomitant medications used for rescue should be reported in the eCRF.

[14] AEs and Concomitant Medications should only be recorded on Day 0 if they result in disqualification (i.e., screen failure) of the subject; otherwise, the AEs and Concomitant Medications applicable to Day 0 should be recorded when the subject returns for Visit 2 (POD1).

[15] Any AEs reported to the site during the POD14 contact or as a result of the POD50/POD78 reminders must be recorded in the source documents. Further assessment of any reported AEs may require an Unscheduled Visit if medically significant or they may be assessed, as appropriate, during Visit 5 (POD15) or Visit 7 (POD85), respectively.

4. SAMPLE SIZE CONSIDERATION

The assumption for the sample size determination was estimated using the Package Inserts of Durezol®, Lotemax® and Inveltys® and results from the APP13007 Phase 2 study (CPN-201). The sample size for the ACC count primary efficacy endpoint is based on the assumption of 26% of subjects in APP13007 group with ACC Count = 0 at POD8 and maintained through POD15 and 12% of subjects in the matching vehicle placebo group. The two-group Chi-square test, with a two-sided significance level of 5% and 92% power, requires 175 subjects per treatment group to detect the difference between APP13007 and placebo.

The same sample size using the assumption of 57% of subjects with Ocular Pain Grade = 0 at POD4 and maintained through POD15 in APP13007 group and 38% of subjects in the placebo group will provide 95% power to detect the treatment difference.

With an estimated 5% dropout rate, this study will randomize approximately 185 subjects per treatment group for a total of approximately 370 subjects.

In the Endothelial Cell Sub-study, a sample size of 80 subjects per treatment group is considered adequate to evaluate the corneal endothelial cell parameters between treatment groups. With a 10% dropout rate, the Sub-study will enroll approximately 88 subjects per treatment group for a total of approximately 176 subjects to be randomized for the Endothelial Cell Sub-study.

5. ANALYSIS POPULATIONS

The analysis populations are defined below.

5.1 Intent-to-Treat (ITT) Population

The ITT population will consist of all subjects who are randomized to the study drug.

Following the ITT principle, subjects will be analyzed according to the treatment assignment at randomization.

5.2 Per-protocol (PP) Population

The PP population will consist of all subjects in the ITT population who (i) receive at last 1 dose of study drug, (ii) do not have major protocol deviations that would impact the evaluation of efficacy, and (iii) have at least 80% overall treatment compliance.

The subjects who are to be excluded from the PP population will be identified prior to database lock and unmasking of the treatment assignment and the reason for exclusion will be documented and listed.

5.3 Safety Population

The safety population will consist of all randomized subjects who receive at least one dose of study drug.

Subjects will be analyzed in the safety analysis according to the treatment actually received.

6. DATA ANALYSIS CONSIDERATIONS

6.1 General Consideration

All statistical analyses and generation of tables, figures, subject data listings, and statistical output will be performed using SAS Version 9.3 or higher.

6.2 General Presentation of Summaries and Analyses

Descriptive statistics will be displayed to provide an overview of the study results. For categorical variables, the number and percentage of subjects in each category will be presented. Unless otherwise noted, all percentages will be displayed to 1 decimal place. No percentage will be displayed for zero counts, and no decimal will be presented when the percentage is 100%. For continuous variables, descriptive statistics will include number of subjects with available measurements (n), mean, standard deviation, median, first quartile (Q1), third quartile (Q3), minimum, and maximum.

Decimal places for descriptive statistics will apply the following rules unless otherwise stated:

- "n" will be an integer
- Mean, standard deviation, and median will use one additional decimal place compared to the original value
- Minimum and maximum will have the same number of decimal places as the original value

Continuous variables will be examined to ensure that they meet the required assumptions for the intended statistical analysis method. If the statistical assumptions are violated, alternative analytical methods, such as nonparametric statistics, will be used.

Unless otherwise specified, all statistical tests will be two-sided and the statistical significance will be tested at the 5% level ($\alpha = 0.05$). Statistical tests of efficacy variables will be presented as two-sided p-values rounded to three decimal places. P-values less than 0.001 will be presented as "<0.001" and p-values greater than 0.999 will be presented as ">0.999".

6.3 Data Handling Rules

6.3.1 Baseline Values

Baseline values is defined as the values obtained at the most recent assessment prior to the first dose of the study drug. Both scheduled and unscheduled visits will be considered.

Screening values will be considered as the baseline values when the change from screening is of interest.

6.3.2 Study Eye

Each subject's study eye is defined as the eye that undergoes cataract surgery in the study.

6.3.3 Non-Study Eye

Each subject's non-study eye is defined as the eye that does not have cataract surgery in the study.

6.3.4 Study Day, End of Main Study (EOMS) and End of Sub-Study (EOSS)

Study Day for each subject is calculated relative to the date of the first dose of study drug:

- Study Day = Visit Date/Event Date - Date of First Dose +1
  When the Visit Date/Event Date is on or after the Date of First Dose
- Study Day = Visit Date/Event Date - Date of First Dose
  When the Visit Date/Event Date is prior to the Date of First Dose

Study Day will be used to define analysis windows for efficacy analyses and to evaluate the timing of events or measurements occurring relative to the first dose of study drug.

Study Day '-1' corresponds to Surgery Day 0 and Study Days '-29' to '-2' correspond to Screening Visit (Days -28 to -1) as shown in the Schedule of Events (Table 2).

EOMS will be either Visit 6/POD22 for all randomized subjects who complete the Main study or the Early Termination/Withdrawal visit for subjects who discontinue the Main study prior to Visit 6/POD22.

EOSS for the subjects in the Endothelial Cell Sub-study will be either Visit 7/POD85 for subjects who complete the Sub-study or the Early Termination/Withdrawal visit for subjects who discontinue the Sub-study prior to Visit 7/POD85.

6.3.5 Analysis Visit for Efficacy Analyses

The use of efficacy data collected in the study will be maximized by including the assessments that are performed outside the planned visit window. Each Analysis Visit (POD 4, 8 and 15) will use an analysis window to determine the efficacy data that will be used to derive the efficacy endpoints. The actual Study Day (Section 6.3.4) will be used to define the analysis window. The analysis window for each Analysis Visit is shown in Table 3.

Table 3: Analysis Windows for Efficacy Analysis

Analysis Visit	POD4	POD8	POD15
Study Days in Analysis Window	2 – 6	7 –11	12 – 17 or Scheduled Visit*

* Only for subjects who (i) complete at least 14 days of dosing, (ii) do not use rescue medication and (iii) have a scheduled POD15 visit after Study Day 17.

If the efficacy assessments are performed at unscheduled visits occurring after Visit 2/POD1 and before Visit 5/POD15, the date of the unscheduled visits will also be used to determine the appropriate analysis window.

The efficacy assessments performed after two days following the last dose of study drug will not be used when the subjects have administered less than 14 days of study drug.

When multiple efficacy assessments fall within the same analysis window for an Analysis Visit (see Table 3), the following rules will be applied:

- If two scheduled assessments fall within the same analysis window for an Analysis Visit and one of the Analysis Visits (either before or after the Analysis Visit with two scheduled assessments) has no scheduled assessment, then the scheduled assessment data will be used for the Analysis Visit without an assessment. For example, when a subject has a scheduled POD4 visit at Study Day 3 and a scheduled POD8 visit at Study Day 6, the Analysis Visit POD4 would have two scheduled assessments and the Analysis Visit POD8 would have no data. In this case, the scheduled POD8 visit assessments will be used for the Analysis Visit POD 8.

- If one scheduled assessment and at least one unscheduled assessment fall within the same analysis window for an Analysis Visit, the latest value in the analysis window will be used for all relevant efficacy analyses.

The definition of the analysis window for each Analysis Visit for the efficacy analyses will be re-examined prior to database lock. If there is a need to adjust the analysis window in Table 3, the SAP will be amended to document the changes.

6.4 Statistical/Analytical Issues

6.4.1 Adjustments for Covariates

The analysis of the continuous secondary efficacy endpoints will be adjusted for baseline values as a covariate in the analyses of covariance (ANCOVA).

6.4.2 Rescued Subjects

Any subject not responding to the study drug because of lack of efficacy at any time after randomization at Visit 2/POD1 may be rescued and placed on an appropriate alternative therapy determined by the Investigator.

The efficacy assessments performed after starting rescue medication will be excluded from the efficacy analyses.

For the primary efficacy endpoints, subjects who are rescued at any time after the first dose of study drug and before the efficacy assessments at POD15 will be considered as treatment failures (Non-responders). The same approach will be applied to derive the secondary endpoint of sustained ACF grade =0.

For both categorical and continuous secondary efficacy endpoints of ACC grade, ocular pain grade and ACF grade, the last observation carried forward (LOCF) approach will be used to impute the data for each Analysis Visit after starting rescue medication.

6.4.3 Handling Dropouts or Missing Data

6.4.3.1 Imputation of Missing Efficacy Data

The missing data handling rule for the study eye will be applied for the efficacy endpoints.

Missing data from subjects who discontinue the study before POD15 assessments without taking rescue medication:

For subjects who prematurely discontinue the study without taking rescue medication, the LOCF approach will be used to impute the missing data. The last observation will be the last assessment value after the first dose of study drug and up to two days following the last dose of study drug.

Missing data from subjects who discontinue the study before POD15 assessments and take rescue medication before POD15 assessments:

For both categorical and continuous secondary efficacy endpoints of ACC grade, ocular pain grade and ACF grade, subjects who take rescue medication before POD15 assessments and prematurely discontinue the study, the LOCF approach will be used to impute the missing data. The last observation will be the last assessment value after the first dose of study drug and prior to starting rescue medication.

Intermittent missing data:

The likelihood of having intermittent missing data is low. For subjects with intermittent missing data for efficacy endpoints, the LOCF approach will be applied to impute the missing data, i.e., using the data collected from the most recent prior visit after the first dose of study drug.

If no data can be carried forward (i.e., missing assessments at POD 4 visit or no available post-baseline assessments), missing data will be treated as missing for the continuous endpoints and will be considered as 'Non-responder' for the categorical endpoints.

6.4.3.2 Imputation of Partial Dates for Birthday, AEs, and Medications

The day of birth date will not be collected in order to protect subjects' privacy. To calculate the age from birth date, the day will be assigned as the 1st day of the birth month.

For analysis of AEs and medications (other than the study drug), a complete date should be established in order to determine treatment emergent AEs (TEAEs) or concomitant medications. The imputation rule of partial dates will be applied for missing components of partially-reported start and stop dates for AEs and for medication use.

Partial start dates of AE and medication will be imputed as follow:

- If only the month and year are reported and the month and year of the start date is not the same as the month and year of the date of first dose of study drug, then use the first day of the month.

- If only the month and year are reported and the month and year of start date is the same as the month and year of the date of the first dose of study drug, then use the date of first dose.
- If only the year is reported, and the year of the start date is not the same as the year of first dose of study drug, then use the January 1st as the start day and month.
- If only the year is reported, and the year of the start date is the same as the year of first dose of study drug, then use the date of first dose.
- If the start date is completely unknown and the stop date is partially known or not prior to the date of first dose of study drug, then use the date of first dose.
- If the imputed start date is after the known stop date, set the start date to be the same as the stop date.

Partial stop dates of AE and medication will be imputed as follow:

- If only the month and year are reported, then use the last day of the month
- If only the year is reported, then use December 31st of that year

If the unknown dates cannot be used to determine whether an AE is treatment emergent or a medication is concomitant, the AE will be considered as treatment emergent or the medication will be considered as concomitant.

In subject data listings, birthday, start and stop date of AEs or medications (other than study drug) will be displayed as reported (i.e., no imputed values will be displayed in data listings).

6.4.4 Handling of Dropouts Due to the COVID-19 Pandemic

The protocol Appendix A describes the Early Termination/Withdrawal procedures that may be implemented because of the COVID-19 pandemic. Subjects who discontinue the study due to COVID-19 will follow the imputation rules described in Section 6.4.3.1 to impute the missing efficacy data.

6.4.5 Multicenter Studies

The randomization will be stratified by study site. No study sites will be pooled for analysis purposes, as the efficacy analyses will not be adjusted for study site differences. If there is a potential site issue identified, an exploratory analysis may be performed to adjust for 'study site' in the analysis of primary efficacy endpoints.

6.4.6 Multiple Comparisons/Multiplicity

Since the comparisons of the primary efficacy endpoints will be performed in the pre-specified sequential order, the fixed-sequence hierarchical testing approach will be used to adjust for multiple comparisons. These endpoints will be tested in the sequence with the rule that once a

p-value exceeds 0.05, the endpoint further down in the sequence will not be claimed for statistical significance.

6.4.7 Subgroup Analyses

The primary efficacy endpoints will be evaluated for subgroups of interest, including:

- Age (< 65 or ≥ 65 years)
- Race (White or Non-White)
- Gender
- Iris color (Blue, Brown or Other)

Subgroup summary will be performed using the ITT population for the primary efficacy endpoints only if the number of subjects in a subgroup is appropriate. No statistical comparisons will be conducted.

7. STUDY POPULATION CHARACTERISTICS

7.1 Subject Disposition

Summaries of the number of subjects screened, the number of screen failures, the number of subjects randomized and the number of subjects randomized in the Sub-study will be produced for all screened subjects.

All randomized subjects will be tabulated by treatment group and study site. Randomized subjects in the Sub-study will also be tabulated by treatment group and study site.

The number of subjects in each analysis population (ITT, PP and Safety) will be tabulated by treatment group for all randomized subjects. The number of subjects in the Safety population will be tabulated for subjects in the Sub-study.

The number and percentage of subjects who complete the study and who prematurely discontinue the study, along with the reason for withdrawal, will be tabulated by treatment group for the ITT population.

The number and percentage of subjects in the Sub-study who complete the Sub-study and who prematurely discontinue the Sub-study, along with the reason for withdrawal, will be tabulated by treatment group for the ITT population.

In addition, the numbers and percentages of subjects who discontinue the study drug before completing the 14-days of dosing and the reason for discontinuing the study drug will be tabulated by treatment group using the Safety population.

Disposition data for all screened subjects will be listed.

7.2 Protocol Deviations

Protocol deviations will be collected in the eCRF. The protocol deviation data will be reviewed for major protocol deviations by the clinical team prior to database lock and unmasking of the study treatment.

The subjects with major protocol deviations including the category of the major protocol deviations will be summarized by treatment group for the ITT population. The number and percentage of subjects excluded from the PP population and the reason for exclusion will be tabulated by treatment group for the ITT population.

The protocol deviation data will be listed. The data listing will include the type of deviation, the category of the deviation (major/minor), the status of being excluded from the PP population (yes/no) and reason for exclusion.

A data listing of subjects who do not meet the inclusion and exclusion criteria will be provided.

8. DEMOGRAPHICS AND BASELINE CHARACTERISTICS

8.1 Demographics and Baseline Characteristics

Demographic data, including age, age category (< 65 or ≥ 65 years), gender, race, ethnicity, iris color, study eye (OD or OS) will be summarized by treatment group and overall. In addition, a summary of the demographic data for the subjects in the Sub-study will be presented.

Demographic and baseline characteristics data, including the data collected on the surgery day (Day 0), will be listed in data listings. Data of contact lens use will be listed for the subjects in the Sub-study.

8.2 Medical/Surgical History

General medical and surgical history, and ocular medical and surgical history reported in eCRF will be coded using the Medical Dictionary for Regulatory Activities (MedDRA version 23.1 - September 2020). General medical and surgical history will be summarized by system organ class (SOC) and preferred term for past and current medical conditions separately. Subjects reporting more than one medical condition in a SOC will be counted only once in that SOC. Ocular medical and surgical history will be summarized by SOC and preferred term for the study eye and non-study eye separately.

Data listings of general medical and surgical history, and ocular medical and surgical history will be provided.

8.3 Prior and Concomitant Medications

Prior and concomitant medications, including rescue medications, will be coded using the World Health Organization (WHO) Drug Dictionary (B3 WHO Drug Global - September 2020). When medications cannot be coded, the name entered in the eCRF will be reported.

A summary of concomitant medications taken during the course of the study will be tabulated by Anatomical Therapeutic Chemical (ATC) Classification and WHO drug name. The summary will exclude prior medications with a stop date prior to the date of first dose of the study drug or follow-up medications with a start date after the last day of the Main study (EOMS). Medications used as part of the routine surgical procedure and rescue medications will be summarized separately.

All prior and concomitant medications will be presented in a data listing.

9. TREATMENT COMPLIANCE

Overall treatment compliance per subject for the study eye is defined as:

Treatment compliance (%) = [Total number of doses instilled correctly / (Actual treatment duration) x 2] x100,

where the actual treatment duration is calculated as the number of days between the first dose date and last dose date of study drug.

The treatment compliance will be summarized using descriptive statistics for the Safety population. In addition, the overall treatment compliance will be further categorized as < 80%, 80% – 100% and > 100%, and the number and percentage of subjects with compliance in each category will be presented.

Subject dosing diary data will be listed.

10. EFFICACY ANALYSES

All efficacy analyses will be performed using the ITT population. In addition, analyses of the primary efficacy endpoints will be performed using the PP population as a sensitivity analysis. All efficacy analyses and summaries will be based on assessments in the study eye for each subject.

The data for subjects who are rescued at any time after the first dose of study drug and before the efficacy assessments at POD15 will be handled as descried in Sections 6.4.2 and 6.4.3.1. The data for subjects who prematurely discontinue the study without taking any rescue medications will be handled as descried in Section 6.4.3.1.

The Analysis Visits (PODs 4, 8 and 15) defined in Section 6.3.5 will be employed in the efficacy analyses.

Baseline values for the efficacy endpoints are defined as the assessment values obtained at POD1 pre-dose.

All efficacy data will be presented in listings.

10.1 Analyses of Primary Efficacy Endpoints

10.1.1 Primary Efficacy Endpoints

The primary efficacy endpoints are:

- The proportion of subjects with ACC count = 0 (ACC grade = 0) at POD8, maintained through POD15
- The proportion of subjects with Ocular Pain grade = 0 at POD4, maintained through POD15

The ACC count will be graded as shown below:

Grade	0	1	2	3	4
ACC Count	0 cell	1-5 cells	6-15 cells	16-30 cells	> 30 cells

The subject-rated Ocular Pain will be graded as follow:

Grade	Description
0	None: No pain.
1	Minimal: Presence of minimal throbbing or aching pain (expected following cataract surgery).
2	Mild: Presence of mild throbbing or aching pain, easily tolerated.
3	Moderate: Presence of moderate throbbing or aching pain leading to the desire to use an analgesic.
4	Severe: Presence of severe throbbing or aching pain that is not tolerable

10.1.2 Primary Analysis

The Pearson's Chi-square test will be used to test the null hypothesis that there is no difference between treatment groups for the primary efficacy endpoints:

1. The proportion of subjects with ACC count = 0 (ACC grade = 0) at POD8, maintained through POD15
2. The proportion of subjects with Ocular Pain grade = 0 at POD4, maintained through POD15

Since the treatment comparisons of the primary efficacy endpoints are in sequential order, the fixed-sequence hierarchical testing approach will be used to adjust for multiple comparisons. The primary analysis will first compare the proportion of subjects with ACC count = 0 (ACC grade = 0) at POD8, maintained through POD15, between APP13007 and placebo. If the test is statistically significant at the 2-sided $\alpha = 0.05$ level in favor of APP13007, the comparison of the

proportion of subjects with Ocular Pain grade = 0 at POD4, maintained through POD15, between APP13007 and placebo will be tested at the two-sided $\alpha = 0.05$ level.

Under the hierarchical testing scheme, once the two-sided p-value exceeds 0.05, the endpoint further down in the sequence will not be claimed for statistical significance.

The tabulated summary of the two endpoints will include the Responder (Response = Yes) and Non-responder (Response = No) for ACC count = 0 (ACC grade = 0) at POD8, maintained through POD15, or for Ocular Pain grade = 0 at POD4, maintained through POD15, and the 95% confidence interval (CI) for Responder. The treatment difference of the Responder rates with the associated 95% CI will be presented. The Response will be further categorized as:

Yes (Responder):

- Yes – Without imputed data
- Yes – With imputed data

No (Non-responder):

- No – With Rescue Medication Use
- No – Without Rescue Medication Use
- No – With imputed data

10.1.3 Sensitivity Analyses

Sensitivity analyses will be performed to confirm the robustness of the primary efficacy analysis results:

1. Analysis of the primary endpoints will be performed using the PP population.
2. "Completed-Case" analysis of the primary endpoints will be performed using the subgroup of Completers based on the ITT population. Completers are defined as the subjects who complete the study and have the data for the ACC count and ocular pain grade assessments at all visits up to POD15.
3. "Observed-Case" analysis of the primary endpoints will be performed using the ITT population and the observed data for subjects who miss one of the assessments used to determine the primary endpoints without taking rescue medication. The subjects with missing data will be considered as treatment failures (Non-responders).
4. "Worst-Case in the Analysis Window" analysis of the primary endpoints will be performed using the ITT population and using the worst Response at PODs 4, 8 and 15 when multiple efficacy assessments fall within the same analysis window for each Analysis Visit.
5. If more than 5% of data are missing for determining the primary efficacy endpoints in any treatment group, a tipping point analysis will be performed when the statistical significance of a treatment difference between two groups has been claimed for each of the two primary

endpoints. Missing data for subjects who take a rescue medication will not be considered as 'missing' since the subjects will have been assigned as treatment failures (Non-responders).

The tipping point analysis of the primary endpoints will be performed using the ITT population to determine the number of subjects with imputed data in the placebo group whose response status has to be changed from Non-Responder to Responder in order to make the treatment difference between the two treatment groups no longer statistically significant.

10.1.4 Additional Analysis

The primary efficacy endpoints will be analyzed using the data collected up to POD15. The rescued subjects will not be considered as treatment failures (Non-responders) for this analysis. All subjects' data collected up to POD15, including the data from subjects who take rescue medication, will be used to analyze the primary efficacy endpoints. Only observed data will be included to derive the primary efficacy endpoints. For the primary endpoint of ACC grade, subjects who miss one of POD 8 and POD15 assessments will be considered as treatment failures (Non-responders). For the primary endpoint of ocular pain grade, subjects who miss one of PODs 4, 8 and 15 assessments will be considered as treatment failures (Non-responders). The Pearson's Chi-square test will be used to test the treatment difference.

10.2 Analyses of Secondary Efficacy Endpoints

10.2.1 Secondary Efficacy Endpoints

The secondary efficacy endpoints are:

- Proportion of subjects with ACC count = 0 (ACC grade = 0) at PODs 4, 8 and 15
- Proportion of subjects with Ocular Pain grade = 0 at PODs 4, 8 and 15
- Proportion of subjects with ACF grade = 0 at POD8 maintained through POD15
- Proportion of subjects with ACF grade = 0 at PODs 4, 8 and 15
- Mean change from baseline in ACC grade at PODs 4, 8, and 15
- Mean change-from baseline in Ocular Pain grade at PODs 4, 8 and 15
- Mean change from baseline in ACF grade on PODs 4, 8 and 15
- Number of subjects rescued on or prior to each visit and overall
- Mean change from baseline in best corrected visual acuity (BCVA) by pinhole method using an ETDRS chart at PODs 4, 8 and 15

The ACC count and Ocular Pain grade will be graded using the same grading scale described for primary efficacy endpoints (Section 10.1.1).

The ACF will be graded as follow:

Grade	Description
0	None
1	Faint
2	Moderate (iris and lens details clear)
3	Marked (iris and lens details hazy)
4	Intense (fibrin or plastic aqueous)

Subjects who meet the rescue criteria may be rescued and placed on an appropriate alternative therapy as determined by the Investigator. The rescue criteria are provided in the protocol Section 9.4.

The ETDRS visual acuity (logMAR score) will be calculated as follows using Original EDTRS Chart 1 and Chart 2:

1. Determine the last row where the subject can correctly identify at least one (1) letter in that row. This is the base logMAR line.
2. Determine the log score for the base logMAR line.
3. Add 0.02 (T = 0.02) log units for every letter that is incorrectly identified up to and including the base logMAR line.

10.2.2 Analysis of Secondary Efficacy Endpoints

10.2.2.1 Analysis of Categorical Endpoints of ACC, Ocular Pain and ACF

The secondary efficacy endpoints (categorical endpoints) of ACC grade, Ocular Pain grade and ACF grade will be analyzed and summarized in the same manner as described for the primary efficacy endpoints (Section 10.1.2). The imputation for missing values for the categorical endpoints is described in Section 6.4.3.1. The proportion of subjects with ACC grade = 0, Ocular Pain grade = 0, and ACF grade = 0 at PODs 4, 8, and 15 will be plotted separately for each of these endpoints.

In addition, the ACC grade, Ocular Pain grade and ACF grade will be tabulated, including the number and percentage of subjects in each grade category, using the observed data only.

10.2.2.2 Analysis of Continuous Endpoints of ACC, Ocular Pain, ACF and BCVA

Mean change from baseline in ACC grade, Ocular Pain grade, ACF grade and BCVA at PODs 4, 8 and 15 will be analyzed using an analysis of covariance (ANCOVA). The ANCOVA model will include treatment as a fixed effect and baseline as a covariate. The imputation for missing values for the continuous endpoints is described in Section 6.4.3.1.

The values of the endpoints and change from baseline at PODs 4, 8 and 15 will be summarized by treatment group using descriptive statistics, including 95% CI for the mean of the change-from-baseline. The adjusted mean of the change from baseline and the treatment difference of adjusted means with associated 95% CI from ANCOVA will be presented. The mean change from baseline with 95% CI at PODs 4, 8 and 15 will be plotted.

In addition, the ACC grade, Ocular Pain grade, ACF grade and BCVA, and change from baseline will be summarized descriptively using the observed data only.

10.2.2.3 Analysis of Endpoint of Rescue Medication Use

The overall number of subjects rescued during the treatment period will be compared between treatment groups using the Pearson Chi-square test. "Rescued during treatment period" is defined as use of rescue medications during the 14-day study drug treatment period. When the treatment duration of study drug is < 14 days, use of rescue medications will be excluded from the analysis when rescue medications are started > 2 days after the last dose of study drug.

In addition, the cumulative number of subjects rescued at PODs 4, 8, and 15 will be summarized by treatment group and compared between treatment groups using the Pearson Chi-square test at each Analysis Visit. In addition, the number and percentage of subjects rescued in each category of criteria for rescue will be presented for the overall study and at PODs 4, 8, and 15. If multiple rescue medications are used by a subject, only the first time a rescue medication is used will be included in the analysis and summary.

11. SAFETY ANALYSES

The extent of exposure and all safety endpoints will be summarized using the Safety population. For all safety endpoints, the observed data and scheduled visits will be used for summary statistics. No imputation of missing data will be employed.

11.1 Extent of Exposure

Exposure to study drug will be summarized by duration (days) on study drug (the number of days between the first dose date and last dose date of study drug) and total number of doses that are instilled correctly in the study eye using descriptive statistics for all subjects in the Safety population and subjects in the Sub-Study. In addition, the duration on study drug will be categorized as 1– 4 days, 5 – 8 days, and 9 – 13 days, and ≥ 14 days, and the number and percentage of subjects in each category will be presented for all subjects in the Safety population and subjects in the Sub-Study. The number of doses received per subject will also be categorized as < 8 doses, 8 – < 16 doses, 16 – < 28 doses, = 28 doses, and >28 doses, and the number and percentage of subjects in each category will be presented by treatment group for all subjects in the Safety population and subjects in the Sub-Study.

If the date of last dose is missing, the date of the last scheduled or unscheduled visit will be used as the date of last dose to calculate the treatment duration.

11.2 Adverse Events

Non-serious AEs occurring from the start of study drug administration until EOMS for the subjects in the Main study only or until EOSS for subjects in the Sub-study will be reported in the eCRF. Serious AEs (SAEs) occurring after signing the informed consent form until EOMS for the subjects in the Main study only or until EOSS for subjects in the Sub-study will be reported in the eCRF. All AEs will be coded using MedDRA version 23.1 - September 2020, and classified by SOC and preferred term.

All AEs occurring from the start of study drug administration through the last day of participation in the Main study (EOMS) are considered as TEAEs.

An overall TEAE summary by treatment group will be presented by the number of events and the number and percentage of subjects experiencing one or more events, including all TEAEs, treatment-related TEAEs, treatment-emergent SAEs, severe TEAEs, TEAEs leading to discontinuation, and death.

The number and percent of subjects reporting one or more TEAEs and the number of TEAEs will be tabulated by SOC, preferred term, and treatment group for all TEAEs. Results will be displayed in order of decreasing frequency based on the occurrence rate in the APP13007 group, both across SOC and within each SOC term. Summaries of all ocular TEAEs, ocular TEAEs in the study eye, ocular TEAEs in the non-study eye, all non-ocular TEAEs, TEAEs related to study drug, ocular TEAEs related to study drug in the study eye, non-ocular TEAEs related to study drug, treatment-emergent SAEs, SAEs related to study drug and TEAEs leading to study discontinuation will also be presented in the same manner. The number and percent of subjects reporting one or more TEAEs will also be summarized by maximum severity for all TEAEs, ocular TEAEs in the study eye and non-ocular TEAEs.

The relationship of TEAEs will be determined by the relationship to study drug and/or to the ocular surgical procedure. Ocular TEAEs related to both study drug and surgery or related to surgery only will be summarized separately.

In addition, the incidence of TEAEs occurring in at least 5% of subjects in any treatment group and incidence of non-serious TEAEs above the threshold of 5% of subjects in any treatment group (for data transparency reporting) will be presented.

For summaries by severity of TEAEs, the most severe occurrence for a particular preferred term will be used for a given subject. AEs with missing severity will be considered as ‘Severe’ events for summary purposes, but will be presented as missing in the AE listings.

A TEAE related to study drug is defined as a TEAE with a “Possible”, “Probable” and “Definite” relationship to study drug as defined in protocol Section 8.3.2. These three relationships will be classified as “Related”. For summaries of TEAEs related to study drug, the most related occurrence for a particular preferred term will be used for a given subject. AEs with missing relationship to study drug or surgery will be considered as “Related” for summary purposes, but will be presented as missing in the AE listings.

AEs occurring between EOMS and EOSS for subjects in the Sub-study will be summarized by SOC, preferred term, and treatment group.

All AEs will be listed in a data listing. All SAEs (including SAEs for all subjects who sign the informed consent), AEs leading to study discontinuation, and deaths will be listed separately.

A serious and unexpected suspected adverse reaction (SUSAR) is defined in the protocol Section 8.2. The SUSARs will be summarized and listed.

11.3 Other Safety Endpoints

The ophthalmic assessments for safety include IOP measurement using Goldmann applanation tonometry, ETDRS assessment of best corrected visual acuity by the Pinhole method, Slit Lamp biomicroscopy assessment of the relevant signs of inflammation, and dilated indirect ophthalmoscopy assessment. The safety assessments will be collected up to EOMS (POD22 or Early Termination before POD22).

11.3.1 Intraocular Pressure

IOP assessments will be performed from Screening through EOMS for the study eye. IOP assessments will be performed at Screening and EOMS for the non-study eye.

For the study eye, the IOP data and change from baseline (POD1 pre-dose) at each post-surgery scheduled visit through EOMS will be summarized by treatment group using descriptive statistics, including 95% CI for the mean of change from baseline. The IOP change from Screening to each scheduled post-surgery visit through EOMS for the study eye will be summarized to evaluate any potential impact from IOP lowering medication use on the surgery day (Day 0). A box and whisker plot will be presented for the IOP change from baseline through EOMS and for the IOP change from Screening through EOMS for the study eye. The IOP change from POD15 to POD22 for non-rescued subjects who complete the study will be summarized for the study eye.

The IOP increase from baseline and increase from Screening will be categorized as ≤0, 1-5, 6-10, >10 (mmHg). The number and percentage of subjects in each category will be tabulated at each post-surgery visit for the study eye. In addition, subjects with an IOP ≥ 21 mmHg and an increase > 10 mmHg from baseline, and subjects with an IOP > 30 mmHg at any time following initiation of study drug will be summarized and listed for the study eye.

The IOP data collected after taking rescue medication will be excluded from the summary tables and plots for the study eye.

The IOP data at Screening and EOMS, and change from Screening to EOMS for the non-study eye will be summarized using descriptive statistics.

All IOP data, including data collected after taking rescue medication, will be presented in a data listing.

11.3.2 Best Corrected Visual Acuity

Since the BCVA endpoint will also be assessed for efficacy, this endpoint has been descripted in the Section 10.2.1. The assessments for the study eye will be performed from Screening through EOMS for safety evaluation. The assessment for the non-study eye will be performed at Screening and EOMS.

The BCVA LogMAR scores and change from baseline (POD1 pre-dose) will be summarized descriptively by treatment group at each post-surgery scheduled visit through EOMS for the study eye. The BCVA base LogMAR scores change from baseline will be classified as ≤ 0, $0 < - < 0.2$ and ≥ 0.2, which are equivalent to ≤ 0 line (visual acuity improved), $0 < - < 2$ lines, and ≥ 2 lines (visual acuity worsened). The number and percentage of subjects in each category will tabulated at each post-surgery scheduled visit for the study eye.

The BCVA LogMAR scores collected after taking rescue medication will be excluded from the summary tables for the study eye.

The BCVA LogMAR scores at Screening and EOMS, and change from Screening to EOMS for the non-study eye will be summarized using descriptive statistics.

All BCVA data, including data collected after taking rescue medication, will be presented in a listing.

11.3.3 Slit Lamp Biomicroscopy

Slit Lamp biomicroscopy assessments will evaluate corneal edema, ciliary flush, bulbar conjunctival injection. The assessments for the study eye will be performed from Screening through EOMS. The assessments for the non-study eye will be performed at Screening and EOMS. The following grades will be used for the assessments.

Grade	Description
0	Absent
1	Mild
2	Moderate
3	Severe

The number and percentage of subjects in each grade category of the assessments will be tabulated by treatment group at each post-surgery scheduled visit through EOMS for the study eye.

A shift table of assessment grades from Screening to EOMS for both eyes will be presented by treatment group.

In addition, the non-study eye lens status (phakic, non-phakic or pseudophakic) will be assessed at Screening. The number and percentage of subjects in each status category will be tabulated.

The data of the biomicroscopy assessments for safety evaluation will be presented in a data listing.

11.3.4 Dilated Indirect Ophthalmoscopy

A dilated indirect ophthalmoscopic examination will be performed at Screening and EOMS for both eyes to evaluate the vitreous, retina, macula, choroid, and optic nerve with cup/disc ratio and will note normal/abnormal findings.

A shift table from Screening to EOMS for each ophthalmoscopic parameter, except for the cup/disc ratio, will be presented by treatment group for both eyes. The cup/disc ratio and change from Screening to EOMS will be summarized descriptively for both eyes.

For the non-study eye only, when the non-study eye is reported as 'Phakic' at the Screening Visit, the lens will be assessed for the presence or absence of a cataract. If a cataract is present, it will be classified as Nuclear, Cortical, or Posterior Subcapsular and graded using the guidance provided in the protocol Appendix B. A shift table of the cataract grade from Screening to EOMS for each cataract location will be presented by treatment group.

The data of the dilated indirect ophthalmoscopic examinations will be presented in a data listing.

11.4 Corneal Endothelial Cell Parameters in the Endothelial Cell Sub-study

Corneal endothelial cell parameters will be measured by a central reading center from the images obtained using a specular microscope. Measurements of corneal endothelial cell density (units: cell/mm^2), percent hexagonality (units: % of cells with hexagonal shape) and coefficient of variation in the sizes of the endothelial cells (units: % variation in size between endothelial cells) will be performed for the study eye at Visit 1/Screening, Visit 6/POD22, Visit 7/POD85 and Early Termination Visit prior to EOSS in the subjects participating in the Sub-study. The measurements of endothelial cell parameters will also be performed at Screening for the non-study eye.

The corneal endothelial cell parameter data for the study eye will be summarized at each assessment visit by treatment group. The mean change from Screening to Visit 7/POD85 with associated 95% CI for the study eye will be tabulated for the three parameters by treatment group, as appropriate. The percent change from Screening to Visit 7/POD85 for corneal endothelial cell density will also be summarized.

The corneal endothelial cell parameter data will be presented in a data listing, including the measurements of endothelial cell parameters at Screening for the non-study eye.

12. INTERIM ANALYSIS

No interim analyses are planned for this study.

13. REFERENCES

None.