# STATISTICAL ANALYSIS PLAN

**VERSION:** 1

**EFFECTIVE DATE:** April 30th, 2020

| VERSION HISTORY | | | |
|---|---|---|---|
| **SAP Number** | **Version Number** | **Effective Date** | **Revision** (Principal change from previous version) |
| 001 | 1 | | Not applicable, new SAP |
| | | | |

## APPROVALS

Prepared _____ Date: 30APR2020
Name: [redacted]
Title: Head, Biostatistics and Data Management

Approved _____ Date: 4May2020
Name: [redacted]
Title: Chief Medical Officer

Approved _____ Date: 4May2020
Name: [redacted]
Title: Chief Executive Officer

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# 1. INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to describe the data analyses and presentation to be performed following the completion of Study CPN-201 entitled "A multicenter, randomized, double-masked, two-part, placebo-controlled, Phase 2A study to evaluate the safety, tolerability and preliminary efficacy of APP13007 for the treatment of inflammation and pain after cataract surgery".

Study endpoints and assessments, planned statistical methods, and derived variables are summarized in this plan. Planned tables, figures, and listings for data presentation are specified. All decisions regarding final analyses, as defined in this SAP document, are made prior to locking the study database.

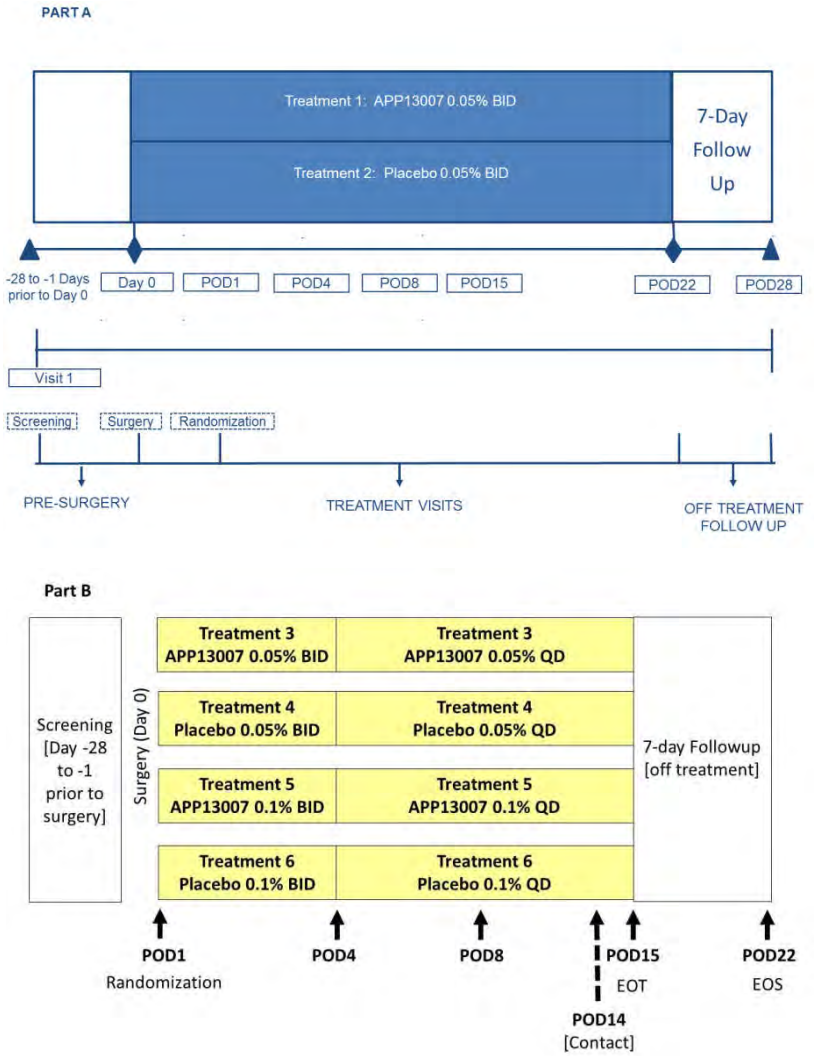
This is an exploratory Phase 2 study for the purpose of dosage regimen selection for Phase 3 studies. Further hypothesis-generating analyses may be performed outside those specified in this SAP.

## 1.1. Study Design

The study design is described by Figure A: Study Schematics in Section 1.1.1, Table B: Treatment Descriptions in Section 1.1.2, and Table C: Schedule of Events in Section 1.1.3.

### 1.1.1. Study Schematics

Figure A




### 1.1.2. Treatment Description for Data Analyses

Three dosing regimens are evaluated, one in Part A and two in Part B. Each has its own matching vehicle placebo.

Data display treatment descriptors with actual treatment dose will be used as shown in Table B below.

Table B: Treatment Descriptions in Data Display

| Treatment ID | Treatment Description | Final Data Display Treatment Description |
|---|---|---|
| Treatment 1: | APP13007 0.05% one drop in the study eye BID for 21 days | APP13007 0.05% BID |
| Treatment 2: | PLACEBO 0.05% one drop in the study eye BID for 21 days | PLACEBO 0.05% BID |
| Treatment 3: | APP13007 0.05% one drop in the study eye BID for 3 days followed by QD for 11 days | APP13007 0.05% BID/QD |
| Treatment 4: | PLACEBO 0.05% one drop in the study eye BID for 3 days followed by QD for 11 days | PLACEBO 0.05% BID/QD |
| Treatment 5: | APP13007 0.1% one drop in the study eye BID for 3 days followed by QD for 11 days | APP13007 0.1% BID/QD |
| Treatment 6: | PLACEBO 0.1% one drop in the study eye BID for 3 days followed by QD for 11 days | PLACEBO 0.1% BID/QD |

### 1.1.3. Schedule of Events

Table C1: Schedule of Events for Part A

| PROCEDURE/ASSESSMENTS[1] | Screening (D-28 to -1) | Surgery[2] Day 0 | POD1[3] | POD4 (±1 Day) | POD8 (±1 Day) | POD15 (±1 Day) | POD21 | EOT/POD22 (+1 Day)[4] | EOS/POD28 (±1 Day)[5] |
|---|---|---|---|---|---|---|---|---|---|
| ICF, Demography, Medical History, FSH[6] (menopausal status) | X | | | | | | | | |
| Determine Eligibility, Review Inclusion/Exclusion Criteria | X | | X | | | | | | |
| Ocular Symptoms Assessment[7] | X | | X | X (R)[16] | X (R) | X (R) | | X (R) | X (R) |
| ETDRS Visual Acuity | X | | X | X (R) | X (R) | X (R) | | X (R) | X (R) |
| Slit Lamp Biomicroscopy[8] | X | | X | X (R) | X (R) | X (R) | | X (R) | X (R) |
| Indirect Ophthalmoscopy (dilated) | X | | | | | | | | X (R) |
| IOP (Goldmann applanation tonometry)[9] | X | | X | X (R) | X (R) | X (R) | | X (R) | X (R) |
| Blood Draw for Safety Lab Parameters (Part A only) | | | X | | | | | X (R) | X (R) |
| Blood Draw for Cortisol (pre-Randomization&POD22) (Part A only) | | | X | | | | | X (R) | |
| Randomization | | | X | | | | | | |
| Dispense Study Drug | | | X | | | | | | |
| Study Drug Dosing for 21 days (POD1 to POD21) | | | X[10] | X | X | X | X | | |
| Dispense Diary Card (with instructions for completion) | | | X | X | X | X | | | |
| Contact Subject[11] | | | | | | | X | | |
| Collect Study Drug | | | | | | | | X (R) | |
| Collect and Check Diary Cards for Accuracy and Compliance | | | | X (R) | X (R) | X (R) | | X (R) | |
| AEs[12] and Concomitant Medications[15] | X | X[13] | X | X (R) | X (R) | X (R) | X[14] | X (R) | X (R) |

[1]Ophthalmic assessments will be performed in the study eye only except at the Screening and EOS/POD28 visits or at subject early termination when the ophthalmic assessments will be performed on both eyes.
[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 (Table 1).
[3]The POD1 visit must be scheduled between 18 to 34 hours following conclusion of surgery on Day 0. All assessments and blood draws done on POD1 are done prior to Randomization.
[4]POD22 is the End-of-Treatment (EOT) visit; subjects who discontinue study drug early (or early termination) should complete the POD22/EOT visit assessments (and indirect ophthalmoscopy) before or during their next scheduled visit.
[5]Subjects will have completed the study following the End-of-Study (EOS) visit on POD28.
[6]FSH should only be measured if needed to confirm postmenopausal status.
[7]Includes assessments of pain and irritation. See Section 8 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 of the ACC number (counted twice), flare grade, bulbar conjunctival injection, sclera - ciliary flush and corneal edema.
[9]IOP should (but not required) be assessed at each visit within ± 2 hr of the time IOP was assessed at the Screening Visit.
[10]The first dose of study drug should be instilled into the study eye at the clinic visit under supervision of clinic staff.
[11] The site must contact the subject via the subject's preferred reliable method to remind him/her not to instill study drug on POD22 and to bring the bottle of study drug and the diary back to the site at the POD22 visit.
[12]See Section 8 for information on how to record AEs and how to determine attributability (relatedness) of AE to study procedures (including cataract surgery) or study drug.
[13]AEs and ConMeds should only be recorded on Day 0 if they result in disqualification (i.e., screen failure) of the subject; otherwise, the AEs and ConMeds applicable to Day 0 should be recorded on POD1 when the subject returns at the POD1 visit.
[14]Any AEs reported to the site during the POD21 contact must be recorded in the source documents. Further assessment of any reported AEs may require an Unscheduled Visit on POD21 if medically significant or they may be assessed, as appropriate, during the POD22 visit.
[15]When concomitant medications are being used for rescue, the appropriate "Rescue" box should be filled in the eCRF.
[16]The designation (R) indicates that the procedure/assessment should be conducted for subjects who have been rescued and withdrawn from study treatment. (See Section 6.3). Subjects who have been rescued will not continue to instill study drug or receive diary cards.

Table C2: Schedule of Events for Part B

| PROCEDURE/ASSESSMENTS[1] | Screening (D-28 to -1) | Surgery[2] Day 0 | POD1[3] | POD4 (±1 Day) | POD8 (±1 Day) | POD14 | EOT/POD15 (+1 Day)[4] | EOS/POD22 (±1 Day)[5] |
|---|---|---|---|---|---|---|---|---|
| ICF, Demography, Medical History, FSH[6] (menopausal status) | X | | | | | | | |
| Determine Eligibility, Review Inclusion/Exclusion Criteria | X | | X | | | | | |
| Ocular Symptoms Assessment[7] | X | | X | X (R)[16] | X (R) | | X (R) | X (R) |
| ETDRS Visual Acuity | X | | X | X (R) | X (R) | | X (R) | X (R) |
| Slit Lamp Biomicroscopy[8] | X | | X | X (R) | X (R) | | X (R) | X (R) |
| Indirect Ophthalmoscopy (dilated) | X | | | | | | | X (R) |
| IOP (Goldmann applanation tonometry)[9] | X | | X | X (R) | X (R) | | X (R) | X (R) |
| Randomization | | | X | | | | | |
| Dispense Study Drug | | | X | | | | | |
| Study Drug Dosing for 14 days (POD1 to POD14) | | | X[10] | X | X | X | | |
| Dispense Diary Card (with instructions for completion) | | | X | X | X | | | |
| Contact Subject[11] | | | | | | X | | |
| Collect Study Drug | | | | | | | X (R) | |
| Collect and Check Diary Cards for Accuracy and Compliance | | | | X (R) | X (R) | | X (R) | |
| AEs[12] and Concomitant Medications[15] | X | X[13] | X | X (R) | X (R) | X[14] | X (R) | X (R) |

[1]Ophthalmic assessments will be performed in the study eye only except at the Screening and EOS/POD22 visits or at subject early termination when the ophthalmic assessments will be performed on both eyes.
[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 (Table 1).
[3]The POD1 visit must be scheduled between 18 to 34 hours following conclusion of surgery on Day 0. All assessments done on POD1 are done prior to Randomization.
[4]POD15 is the End-of-Treatment (EOT) visit in Part B; subjects who discontinue study drug early (or early termination) should complete the POD15/EOT visit assessments (and indirect ophthalmoscopy) before or during their next scheduled visit.
[5]Subjects will have completed Part B the study following the End-of-Study (EOS) visit on POD22.
[6]FSH should only be measured if needed to confirm postmenopausal status.
[7]Includes assessments of pain and irritation. See Section 8 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 of the ACC number (counted twice), flare grade, bulbar conjunctival injection, sclera - ciliary flush and corneal edema.
[9]IOP should (but not required) be assessed at each visit within ± 2 hr of the time IOP was assessed at the Screening Visit.
[10]The first dose of study drug should be instilled into the study eye at the clinic visit under supervision of clinic staff.
[11] The site must contact the subject via the subject's preferred reliable method to remind him/her not to instill study drug on POD15 and to bring the bottle of study drug and the diary back to the site at the POD15 visit.
[12]See Section 8 for information on how to record AEs and how to determine attributability (relatedness) of AE to study procedures (including cataract surgery) or study drug.
[13]AEs and ConMeds should only be recorded on Day 0 if they result in disqualification (i.e., screen failure) of the subject; otherwise, the AEs and ConMeds applicable to Day 0 should be recorded on POD1 when the subject returns at the POD1 visit.
[14]Any AEs reported to the site during the POD14 contact must be recorded in the source documents. Further assessment of any reported AEs may require an Unscheduled Visit on POD14 if medically significant or they may be assessed, as appropriate, during the POD15 visit.
[15]When concomitant medications are being used for rescue, the appropriate "Rescue" box should be filled in the eCRF.
[16]The designation (R) indicates that the procedure/assessment should be conducted for subjects who have been rescued and withdrawn from study treatment. (See Section 6.3). Subjects who have been rescued will not continue to instill study drug or receive diary cards.

## 1.2. Objectives and Endpoints

Table A. Objectives and Endpoints

| OBJECTIVE | ENDPOINT |
|---|---|
| The **primary safety objective** of this study is to investigate the safety and tolerability of APP13007 versus corresponding matching vehicle placebo for the treatment of inflammation and pain through post-operative day (POD) 22 in Part A and POD15 in Part B after cataract surgery. | • Early Treatment Diabetic Retinopathy Study (ETDRS) Best corrected Visual Acuity by pinhole method<br>• Slit-lamp biomicroscopy<br>  ○ Corneal edema<br>  ○ Ciliary flush<br>  ○ Bulbar conjunctival injection<br>• Dilated indirect ophthalmoscopy<br>  ○ Vitreous<br>  ○ Retina<br>  ○ Macula<br>  ○ Choroid<br>  ○ Optic nerve<br>• Intraocular pressure (IOP)<br>• Adverse event (AE) monitoring<br>• Clinical chemistry and hematology parameters (Part A only) (Appendix B)<br>• Serum cortisol concentrations (Part A only) |
| The **primary efficacy objective** of this study is to investigate the preliminary efficacy of APP13007 versus matching vehicle placebo for the treatment of inflammation and pain through POD15 after cataract surgery. | • Anterior chamber cell (ACC) count at POD15<br>• Pain grade at POD15 |
| The **secondary efficacy objective** of this study is to compare the effects on markers of inflammation and pain and visual acuity between active APP13007 and matching vehicle placebo for each dose strength and frequency. | • ACC count at PODs 4, 8 (and 22 for Part A).<br>• Pain grade at PODs 4, 8 (and 22 for Part A)<br>• Anterior chamber flare (ACF) grade at PODs 4, 8, 15 (and 22 for Part A)<br>• ACC grade at PODs 4, 8, 15 (and 22 for Part A).<br>• Use of rescue medication and/or early withdrawal |

| OBJECTIVE | ENDPOINT |
|---|---|
| | • Proportion of subjects with ACC count = 0 at PODs 4, 8, 15 (and 22 for Part A) without receiving rescue medication;<br>• Proportion of subjects who are pain-free at PODs 4, 8, 15 (and 22 for Part A) without receiving rescue medication;<br>• Proportion of subjects with ACF grade = 0 at PODs 4, 8, 15 (and 22 for Part A) without receiving rescue medication<br>• Visual acuity (ETDRS Best corrected Visual Acuity by pinhole method) at PODs 4, 8, 15 (and 22 for Part A) without receiving rescue medication |

## 2. Statistical Hypotheses

No formal hypotheses are being tested.

All reported p-values will be considered exploratory and hypothesis-generating.

## 3. Sample Size Determination

This is a Phase 2a trial to explore dosing regimens, and no formal sample size calculations were used to determine the number of subjects to be enrolled into the trial. The sample size of 21 subjects in each study drug group was selected based on feasibility. Assuming a dropout rate of 5%, approximately 21 subjects will be enrolled into each treatment arm so that approximately 20 subjects per treatment arm would be expected to complete study drug dosing through the POD15 visit.

## 4. Populations for Analyses

The analysis populations are defined as safety population, intent-to-treat population, and per-protocol population.

### 4.1. Safety Population

Safety population consists of all subjects who received at least one dose of study drug.

### 4.2. Intent-to-Treat (ITT) Population

ITT population consists of all subjects who are randomized to a study drug.

### 4.3. Per-Protocol Population

Per-Protocol population consists of all randomized subjects who complete the study drug dosing through POD14 and do not have any major protocol deviations as defined in Section 6.1 that could affect the efficacy endpoints.

## 5. Statistical Analyses

### 5.1. General Consideration

Data analyses will be performed by the Sponsor designee, PharStat, Inc. Raleigh, NC.

Tables and listings will be prepared in accordance with the current International Conference on Harmonization (ICH) Guidelines (ICH E3 Structure and Content of Clinical Study Reports 1996).

Version 9.3 or higher of the SAS system will be used to analyze the data and to generate tables, figures, and listings. All SAS programs prepared to analyze the data will be properly annotated.

The format of this Statistical Analysis Plan follows the TransCelerate BioPharma's template, version Nov. 2018.

#### 5.1.1. General Statistical Analyses

All analyses will be done by each study part separately.

All analysis variables will be summarized descriptively by each active dosing regimen and its matching vehicle placebo group.

Continuous measures will be summarized as mean and standard deviation. In most cases, 95% confidence interval, median, and range will also be provided. Inferential statistics for continuous primary and secondary efficacy endpoints will include Student t-test and/or Mann-Whitney test.

Categorical measures will be summarized by counts. Due to the small sample size, the percentage of subjects will be provided only when it is necessary. The total number for the relevant population and the number of subjects who are still on study drug will be listed with the counts of categorical measures. "On study drug" will be defined in Section 5.1.6.2.

#### 5.1.2. Tables

All tables are organized by study part and by treatment, i.e., two treatments on each table: the active dosing regimen and its matching vehicle placebo. All statistical comparisons are between the active dosing regimen vs. its matching vehicle placebo in each study part separately.

5.1.3. Subject Listings

All supporting data to tables and figures will be sorted and listed by study part, treatment, investigator, subject, and visit.

5.1.4. Reporting Conventions

The information and explanatory notes in the "footer" or bottom of each table and listing will include the following information:

- Date of output generation
- SAS® program name, including the path where the program is stored
- Any other output specific details that require further elaboration
- In general, tables will be formatted with a column displaying findings for all subjects by treatment group in each study part.
- For summary tables, the following reporting convention in Table D will be used unless otherwise stated:

Table D Decimal Places

| | | |
|---|---|---|
| Categorical measures | Counts (n) | None |
| | Percentages (%) | 1 decimal place |
| Continuous measures | n | None |
| | Mean | i+1 decimal places |
| | Median | i+1 decimal places |
| | SD | i+1 decimal places |
| | Min | i decimal places |
| | Max | i decimal places |
| Derived variables | p-values | if <0.001: presented as <0.001 |
| | | if ≥ 0.001: presented to 3 decimal places |

i refers to the number of decimal places reported in the CRF or other appropriate source data for the original data.

5.1.5. Visits, Days, PODs, EOT and EOS

5.1.5.1. Definition of Visits

Based on Tables C1 and C2, Schedule of Events, visits and their nominal days relative to the surgery are further described in Table E below.

**Table E: Visits**

| Visit Number | Visit Name | Notes |
|---|---|---|
| 10 | Screening | Days -28 to -1. Baseline for most safety endpoints |
| 20 | Surgery | Day 0 |
| 30 | POD1 | Randomization and start of study drug.<br>Baseline for efficacy endpoints |
| 40 | POD4 | 3-5 days post-surgery |
| 50 | POD8 | 7-9 days post-surgery |
| 60 | POD15 (Part A only) | 14 -16 days post-surgery for Part A |
| 70 | End of Treatment (EOT)<br>POD22 (Part A)<br>POD15 (Part B) | 1-2 days post last dose of study drug.<br>Part A: 22-23 days post-surgery<br>Part B: 15-16 days post-surgery |
| 80 | End of Study (EOS)<br>POD28 (Part A)<br>POD22 (Part B) | 6-8 days post the last dose of study drug.<br>Part A: 27-29 days post-surgery.<br>Part B: 20-22 days post-surgery |
| 90 | UNSCHEDULED | |

Some subjects may discontinue their study drug before the scheduled EOT. Situations like this will be discussed in the following sections.

5.1.5.2 Visit windows

It is expected that all visits should occur according to the protocol schedule described in Table C1 and Table C2, the Schedule of Events; visits outside of this schedule will be addressed as protocol deviations. A new visit variable, AVISIT, will be defined based on the visit date relative to the date of surgery and a windowing strategy described by Table F. AVISIT will only be used for efficacy variables.

**Table F: Windowing Strategy**:

| Surgery | Day 1 post-surgery | 2-6 days post-surgery | 7-11 days post-surgery | 12-18 days post-surgery | 19-25 days post-surgery | 26+ days post-surgery |
|---|---|---|---|---|---|---|
| Day 0 | POD1 | POD4 | POD8 | POD15 | POD22 | POD28 |

5.1.6. Missing Data and Data Handling Rules

Incomplete dates, missing visits, missing assessments, and situations for subjects who prematurely discontinued study drug are discussed in the following.

5.1.6.1. Incomplete dates for birthday, adverse events, 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 1st of the birth month.

For analysis of AEs and medications, a complete date should be established in order to determine whether AEs or medications as occurring during study drug or not. For the purpose of handling partially reported start and stop dates for AEs or medications, the following algorithm will be applied:

| | |
|---|---|
| Missing start day, but month and year present | If study drug had been taken in the same month and year as the occurrence of the AE/medication, then the start day of the event/medication will be assigned to the day of first dose of study drug.<br>Otherwise the start day will be set to the first day of the month. |
| Missing start day and month, but year present | If study drug had been taken in the same year as the occurrence of the AE/medication, then the start date of the event/medication will be assigned to the date of first dose of study drug.<br>Otherwise the start day and month will be set to 01 January. |
| Missing end day and month, but year present | The end day and month will be set to the date of end of study.<br>However, if trial termination year is greater than the year of the event/medication, then the day and month will be set to 31December.<br>In subject data listings, start and stop date of AEs or medication will be displayed as reported. |

5.1.6.2. Missing data, rescue, last observation carried forward (LOCF)

| | |
|---|---|
| LOCF | The last on study drug assessment is carried forward to impute a later missing value. |
| On study drug | Subjects are considered as being on study drug when they start their first dose until two days after their last dose of the study drug. |

For efficacy analyses of POD1 to POD22 (Part A) and POD1 to POD15 (Part B), LOCF method will be used to impute all assessment values after the subjects that are rescued or early withdrawn and/or have stopped being on study drug to calculate mean, standard deviation, 95% confidence interval, median, Q1, Q3, minimum, and maximum for anterior chamber cell (ACC) count, ACC grade, ACF grade, pain grade, and Best Corrected Visual Acuity.

Therefore, if a subject has an observed POD1 value for an efficacy endpoint, this subject should have observed or imputed values for the same endpoint through POD1 – POD22 for Part A or POD1-POD15 for Part B. Consequently, to avoid confusion, "POD22" will be used in place of "EOT" for Part A and "POD15" for Part B.

LOCF will not be used for "complete" subjects even if they have stopped study drug earlier than POD21 (Part A) and POD14 (Part B).

LOCF will not be used for safety analyses. For safety endpoints, the total number of subjects in the safety population and the summary statistics of all observed data will be calculated for each active dosing regimen and its matching vehicle placebo group for each visit.

Since the eye exams at Screening and EOS visits are evaluated as safety endpoints, the last non-missing observation from the study-eye at post-surgery PODs will not be carried forward to impute missing values at EOS visit for the Screening vs. EOS analyses.

To be clear, in any cases, EOS measurements will not be modified and Screening measurements will not be carried forward.

#### 5.1.7. Baseline Definitions

Baseline is the last observed (without LOCF or any other imputation) assessment prior to the time when the first dose of study drug is administered unless otherwise specified.

Screening will be considered as the baseline for the Screening vs EOS comparison. EOS data will be summarized with Screening data in the same table.

For all other PODs, i.e., POD 1, 4, 8, 15, and 22 (for Part A), POD1, 4, 8, and 15 (for Part B), ocular examinations are carried out for the study eye only. These data will be summarized in the same table for each active dosing regimen and its matching vehicle placebo. The Pre-dose assessment at POD1 will be the baseline.

#### 5.1.8. Change from Baseline

| | |
|---|---|
| Change from baseline (CFB) is calculated as: | CFB value = 'visit' value – baseline value<br>CFB will be indicated as missing, if either the baseline or post-dose value is missing. |

5.1.9. Multiple Assessments at One Time Point

Where multiple assessments are recorded for a particular POD, e.g., ACC counts at the same visit or when two visits fall in the same POD window (**Table F**), the mean of the assessments will be calculated and used in any derivation of summary statistics. All observed data will be listed.

Note, for any efficacy endpoint:

If EOS falls in the same POD window (**Table F**) with another visit, the assessment obtained from that other visit, while the subject is still on study drug, will be used for the efficacy analyses.

If there are no other assessments in the same POD window (**Table F**) while the subject is still on study drug, e.g., within 2 days of the last dose of study drug as defined in 5.1.6.2, the EOS assessment will be used for efficacy analyses.

For any safety categorial endpoint, instead of taking the mean of all assessments within that POD window, the assessment obtained at the latest visit within that POD window will be used for that POD.

EOS assessments will not be modified in any case as mentioned in 5.1.6.2.

5.1.10. Final Analyses

The final analysis will be performed when the last randomized subject has completed the final study visit, the data are monitored and cleaned, and the database has been locked and authorized for analysis. A data review meeting will precede database lock.

5.1.11. Deviations from SAP

Any deviations from the SAP will be documented and a justification given in the clinical study report.

5.2. Subject Disposition

Total number of subjects screened, proportion of screen failures, proportion of randomization failures will be presented in Table 14.1.1.

The total number of subjects for each active dosing regimen and its matching vehicle placebo in each study population, namely, safety, ITT, and per protocol, will also be presented in Table 14.1.1.

Furthermore, the number and proportion of subjects who discontinued study drug prior to POD21 for Part A and POD14 for Part B will be summarized for each treatment according to reason of discontinuation in Table 14.1.1.

All subjects' disposition status information, reasons of screen/randomization failure and discontinuation of study drug prior to POD21 will be presented in Listing 16.2.1.

## 5.3. Primary and Secondary Efficacy Endpoint(s) Analysis

### 5.3.1. Definition of Primary and Secondary Efficacy Endpoint(s)

The **primary efficacy endpoints** are:

- Anterior chamber cell (ACC) count at POD15 (mean of two counts)
- Pain grade at POD15

Pain grade is defined as follows:

| | |
|---|---|
| 0 | None: Absence of 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 | Moderate: Presence of moderate throbbing or aching pain leading to the desire to use an analgesic. |

The **secondary efficacy endpoints** are:

- Anterior chamber cell (ACC) count at PODs 4, 8 (and 22 for Part A), mean of two counts at each POD.
- ACC grade at PODs 4, 8, 15 (and 22 for Part A), mean of two grades at each POD

ACC grade is defined as the following:

| 0 | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| 0 cell | 1-5 cells | 6-15 cells | 16-30 cells | > 30 |

- Pain grade at PODs 4, 8 (and 22 for Part A)
- ACF grade at PODs 4, 8, 15 (and 22 for Part A)

ACF grade is defined as follows:

| ACF Grade | ACF Grade Used for Analyses | Description |
|---|---|---|

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

- Use of rescue medication and/or early withdrawal
- Proportion of subjects with ACC count = 0 (first measurement only) at PODs 4, 8, 15 (and 22 for Part A) without receiving rescue medication;
- Proportion of subjects who are pain-free at PODs 4, 8, 15 (and 22 for Part A) without receiving rescue medication;
- Proportion of subjects with ACF grade = 0 at PODs 4, 8, 15 (and 22 for Part A) without receiving rescue medication
- Visual acuity (ETDRS Best corrected Visual Acuity by pinhole method) at PODs 4, 8, 15 (and 22 for Part A) without receiving rescue medication

See Section 7.2 of the protocol for more details about the definitions of the endpoints.

5.3.2. Main analytical approach

The primary and secondary efficacy endpoints analyses will follow the General Consideration described in Section 5.1.

Efficacy analysis will be performed for the ITT population.

The primary efficacy endpoints and the secondary endpoints will be summarized in the same tables, figures, and listings.

**Rescue and Early Withdrawal:**

Rescue criteria: After randomization

- anterior chamber cells count >30 cells,
- an increase in anterior chamber cell count by > 15 cells from POD1/pre-dose baseline, or
- ≥2 grade of increase in ACF from POD1/pre-dose baseline.

For visits POD4 through EOS, the total number of subjects randomized, number of subjects who are still on study drug, and the number of subjects rescued for each reason and for subjects withdrawn early will be summarized in Table 14.2.1 for each active dosing regimen and its matching vehicle placebo.

The denominator of each proportion is the number of subjects being randomized.

Subjects' rescue and early withdrawn information together with reasons will be presented in Listing 16.2.6.1.

**Inflammation and Best Corrected Visual Acuity (BCVA) endpoints:**

Both eyes at Screening and End of Study (EOS):

Although the tables for these data are numbered 14.**2**.xxx and listed with other efficacy endpoint tables, the analyses of parameters for eye exams at Screening and EOS visits, especially, those for the non-study-eye, are primarily considered as safety analyses and, therefore, they will be carried out for the safety population.

ACC count, ACC grade, pain grade, ACF grade, and ETDRS acuity (logMAR score) will be summarized descriptively for Screening and EOS visits for each active dosing regimen and its matching vehicle placebo. The summary statistics include total number of subjects in the safety population, mean, standard deviation, 95% confidence interval, median, Q1, Q3, minimum, and maximum of observed data. See Tables 14.2.2.1.1-14.2.2.1.4, and 14.2.5.1.

The distribution of ACC, pain, and ACF grades for each treatment group will be described by the frequency within each grade for Screening and EOS visits. See the top part of Tables 14.2.3.1 – 14.2.3.3.

Last non-missing observation from the other PODs will not be carried forward to impute missing values at EOS visit as discussed in Section 5.1.6.2.

Study eye only**:**

ACC count, ACC grade, pain grade, ACF grade, and ETDRS acuity (logMAR score) will be summarized descriptively in Tables 14.2.2.2.1-14.2.2.2.4, and 14.2.5.2 for POD1-22 (Part A) and POD1-15 (Part B) by each active dosing regimen and its matching vehicle placebo. LOCF method will be used to impute all assessments after the subject stopped being on study drug to calculate mean, standard deviation, 95% confidence interval, median, Q1, Q3, minimum, and maximum. On study drug is defined in Section 5.1.6.2**.**

The observed data (without LOCF or any other imputation) when the subjects are still on study drug of above listed endpoints will also be summarized in Tables 14.2.2.3.1 – 14.2.2.3.4, and 14.2.5.3. The treatment difference will also be reflected by the number of subjects that are still on study drug. PODs defined by Table F will be used for calculating the treatment group statistics.

The same statistics will be calculated for CFB of the same endpoints, with POD1 pre-dose measure as the baseline, in Tables 14.2.2.4.1-14.2.2.4.4, and 14.2.5.4. LOCF will be used to impute missing values and all assessments after subjects stopped being on study drug. Statistical comparison between each active dosing regimen and its matching vehicle placebo will be carried out for each visit during POD4 - POD22 (Part A) and POD4 – POD15 (Part B) using t-test and Mann-Whitney non-parametric tests noting that p-values will only be considered descriptive and hypothesis-generating.

These endpoints will also be visually presented in Figures 14.2.2.1, 14.2.2.2, 14.2.5.1, and 14.2.5.2.

The distribution of ACC, pain, and ACF over different grades for each treatment will be described by the frequency and proportion of subjects within each grade for each active dosing regimen and its matching vehicle placebo for each visit during POD4 – POD22 (Part A) and POD4 –POD15 (Part B) in the lower part of Tables 14.2.3.1 – 14.2.3.3 without LOCF. The denominator of the proportion is the number of subjects randomized. The treatment difference will also be reflected by the number of subjects that are still on study drug.

The proportion of subjects with ACC count = 0, pain-free, or ACF grade = 0 without receiving rescue medication will be calculated for each active dosing regimen and its matching vehicle placebo for each visit during POD1 – POD22 (Part A) and POD1 – POD15 (Part B) in Table 14.2.4 and Figure 14.2.4. The denominator will be the total number of subjects randomized in each treatment group. LOCF will be used to impute missing values and all assessments after subjects stopped being on study drug.

All subjects' inflammation and pain information will be presented in Listing 16.2.6.2 and best correct visual acuity information will be presented in Listing 16.2.6.3.

### 5.3.3. Sensitivity analysis

A subset of efficacy analyses will be examined for the per-protocol population as supportive analysis.

Since only first ACC count will be used to define the proportion of subject with ACC count = 0, analyses of using second ACC count and/or a combination of the two counts will be explored.

### 5.3.4. Supplementary Analyses

Exploratory hypothesis-generating analyses may be performed as necessary.

5.3.4.1. Proportions of "Resolved", "Unresolved", and "Early discontinuation of study drug"

To understand the persistence of grade=0 for ACC (the first of two counts), ACF, and pain, proportions of "resolved", "unresolved", and "early discontinuation of study drug" will be calculated for each active dosing regimen and its matching vehicle placebo group at each POD in Table 14.2.4 and Figure 14.2.4

A subject is defined as "Early discontinuation of study drug" at a POD when the subject is not on study drug at that POD. See Section 5.1.6.2 for the definition of on study drug.

A subject's ACC (ACF, or pain) is defined as "Resolved" at a POD when the first of the two ACC counts (grade for ACF and pain) at that POD and all PODs beyond is equal to zero while the subject is still on study drug for all these PODs. Otherwise, the subject is "Unresolved".

For example, if a subject's first of two ACC counts equal to zero at POD8 but the first of two ACC counts >0 at POD15, this subject would be "Unresolved" at both POD8 and POD15.

If a subject's first of two ACC counts >0 at POD22 (Part A) or at POD15 (Part B) this subject cannot be "Resolved" at any POD.

Apparently, a subject having an "Early discontinuation of study drug" can never be "Resolved" at any PODs. More precisely, this subject will be an "Early discontinuation of study drug" for all PODs beyond.

## 5.4. Secondary Efficacy Endpoint(s) Analysis

Secondary efficacy endpoints will be analyzed with the primary efficacy endpoints together. See Section 5.3 for details.

## 5.5. Tertiary/Exploratory Endpoint(s) Analysis

None are planned.

## 5.6. Safety Analyses

Safety data will be analyzed for all subjects in the Safety population.

The safety endpoints are:

- Adverse event (AE)
- Serum cortisol concentrations (Part A)
- Clinical chemistry and hematology parameters (Part A) (Appendix B)
- Intraocular pressure (IOP)
- Early Treatment Diabetic Retinopathy Study (ETDRS)

- Best corrected Visual Acuity by pinhole method
- Slit-lamp biomicroscopy
  - Corneal edema
  - Ciliary flush
  - Bulbar conjunctival injection
- Dilated indirect ophthalmoscopy
  - Vitreous
  - Retina
  - Macula
  - Choroid
  - Optic nerve

See Section 7.2 of the protocol for detail about these endpoints. The analyses of these safety endpoints are described in the following sub-sections.

For all safety endpoints, the total number of subjects in the safety population and the summary statistics of all observed data will be calculated for each active dosing regimen and its matching vehicle placebo group and each visit as defined in the CRF. No imputation will be used.

### 5.6.1. Extent of Exposure

The summary statistics of number of eye drops that were instilled correctly in the study eye during the entire treatment course will be calculated for each active dosing regimen and its matching vehicle placebo group and will be presented in Table 14.1.4. Individual dosing diary will be presented in Listing 16.2.5.1

### 5.6.2. Adverse Events

Adverse events (AE) will be summarized by total number of any AE, number of subjects reporting the AE, ocular AEs (affecting the study eye and/or the non-study eye and/or both eyes, when appropriate), systemic AEs, SAEs, discontinuing study drug due to an AE, by relationship to study drug only, to ocular surgery only, or to both drug and ocular surgery, and by severity. Adverse events will be coded using Medical Dictionary for Regulatory Activities (MedDRA version 22.0 – March 2019) and categorized by system organ class and preferred terms.

See Tables 14.3.1.1 – 14.3.1.3 for details.

All adverse events will be listed by both reported term and MedDRA term in Listing 16.2.7.1 and 16.2.7.2.

All serious and significant adverse events will be listed in Table 14.3.2 and narrated in Table 14.3.3.

5.6.3. Clinical Chemistry and Hematology Parameters (Part A only) (Appendix B)

All laboratory data will be summarized by mean, SD, 95% CI, median, Q1, Q3, minimum, and maximum for POD1 Pre-Dose, EOT, and EOS for the active and its matching vehicle placebo groups in Part A in Table 14.3.5.1. The frequencies of shift from Low, Normal, or High, defined by Covance Laboratory Services, to other categories will also be summarized for both treatments in Table 14.3.5.2. All values will be listed for all subjects in the safety population by treatment for POD1 Pre-Dose, EOT and EOS in Listing 16.2.8.1 and 16.2.8.2. All values that are out of normal range will be listed in Table 14.3.4 and Listing 16.2.8.3.

5.6.4. Serum Cortisol Concentration (Part A only)

Serum cortisol concentration will be summarized in the same way as other laboratory tests for POD1 pre-randomization and EOT for the active and its matching vehicle placebo groups in Part A in Table 14.3.5.3 and 14.3.5.4 and visually presented in Figures 14.3.5.1.

All serum cortisol values and their flags (H or L) defined by Covance Laboratory Services will be listed for all subjects by treatment for Screening and EOT visits in Listing 16.2.8.4. All individual subject values will be visually presented in Figure 14.3.5.2.

5.6.5. Intraocular Pressure

For both eyes at Screening and EOS, the analyses of IOP will follow the methods discussed in Section 5.3.2 for Both eyes at Screening and End of Study (EOS). The results will be presented in the top part of Table 14.3.6.1 and Table 14.3.6.2.

For study eye at POD1-POD22 (Part A) and POD1-POD15 (Part B), the analyses will follow the methods discussed in Section 5.3.2 for "observed data" under Study eye only. The results will be presented in Table 14.3.6.1 and its CFB (Baseline = Screening for EOS; Baseline = POD1/pre-dose for other PODs) for the active and its matching vehicle placebo groups at each visit in Table 14.3.6.2 and visually presented in Figure 14.3.6.1.

The distribution of IOP over the ranges of <10, 10-15, 16-20, 21-25, 25-30, and >30(mmHg) for each treatment will be described by the frequencies in each range in Table 14.3.6.3. The distribution of IOP increase over ranges of ≤0, 1-5, 6-10, 11-15, >15 (mmHg) for the active and its matching vehicle placebo groups will be described by the frequency in each range at each visit in Table 14.3.6.4.

The number of subjects with an IOP ≥ 24 mmHg AND an increase ≥ 10 mmHg from pre-dose baseline, and the number of subjects with an IOP > 30 mmHg at any time following initiation of study drug will be summarized in the adverse event tables, Table 14.3.1.1- 14.3.1.3.

All subjects' intraocular pressure information will be presented in Listing 16.2.9.2 and visually presented in Figure 14.3.6.2.

5.6.6. Visual Acuity Worsening from Baseline

The number of subjects with a visual acuity worsening of ≥ 2 lines (equivalent to ≥ 0.2 logMAR CFB), together with ≤ 0 (≤ 0 logMAR CFB) and in between (0< logMAR CFB < 0.2) at EOS from Screening and at each visit during POD4-POD22 (Part A) and POD4-POD15 (Part B) from POD1/pre-dose visit will be summarized in Table 14.3.6.5.

As mentioned earlier, all subjects' best correct visual acuity information will be presented in Listing 16.2.6.3.

5.6.7. Other Ocular Exams

Ocular symptoms, comfort grading assessment, ophthalmoscopy findings, and slit lamp biomicroscopy results will be categorically summarized.

**Slit Lamp Biomicroscopy**:

The distribution of Bulbar Conjunctival Injection, Sclera – Ciliary Flush, and Corneal Edema over the following categories: Absent, Mild, Moderate, and Severe for each treatment at each visit will be described by the frequencies in each category for each active dosing regimen and its matching vehicle placebo in Tables 14.3.6.6 -14.3.6.8.

All subjects' slit lamp biomicroscopy information will be presented in Listing 16.2.9.3.

**Inflammation Endpoints**:

As mentioned in Section 5.3.2, although the Tables 14.2.2.1, 14.2.3.1, 14.2.3.2, 14.2.3.3, and 14.2.5.1 are listed with other efficacy endpoint tables, the analyses of the eye exam parameters at the Screening and EOS visits, especially those for the non-study-eye, are primarily considered as safety analyses.

**Dilated Indirect Ophthalmoscopy**:

The number of subjects with abnormal vitreous retina, macula, choroid, and optic nerve for each active dosing regimen and its matching vehicle placebo will be summarized for Screening and EOS visits in Table 14.3.6.9 – 14.3.6.13.

Cup-to-Disc Ratio will be summarized by mean, SD, 95% CI, median, Q1, Q3, minimum, and maximum for each active dosing regimen and its matching vehicle placebo at Screening and EOS visits in Table 14.3.6.14.

Lens pathology findings for non-study eye will be summarized in Table 14.3.6.15 for subjects with phakic lens by the total number of subjects with abnormal findings and by abnormal cataract category: Nuclear, Cortical, and Posterior Subcapsular and by cataract Grade 1, 2, and 3 for each active dosing regimen and its matching vehicle placebo at Screening and EOS visits.

All dilated indirect ophthalmoscopy ocular exam data will be presented in Listing 16.2.9.4.

### 5.7. Other Analyses

None are planned.

### 5.8. Interim Analyses

No formal interim analyses are planned for this study.

Masked and, if warranted, unmasked data reviews to determine the progression from Part A to Part B are described in Section 3.3 of the protocol.

## 6. Supporting Documentation

### 6.1. Inclusion/Exclusion criteria

Inclusion and Exclusion criteria and comments will be presented in Listing 16.2.2.1 -16.2.2.3.

### 6.2. Protocol deviation

Major Protocol Deviations are defined as those deviations that have the potential to

(i) affect subject rights, safety and/or wellbeing, and/or
(ii) affect study objectives and/or endpoints assessments.

Only major protocol deviations are documented in the clinical study report (CSR).

All details of protocol deviation cases will be presented in Listing 16.2.2.4.

There will be a separate class of major protocol deviations due to the COVID-19 pandemic in the clinical study report.

Subjects excluded from Per Protocol population will be presented in Listing 16.2.3.

## 6.3. Baseline characteristics and demographics

The Safety population will be the primary population for the summary of demographics. Demographics, including mean and standard deviation of age, count and proportion of gender, race, ethnicity, iris color, study eye (OD or OS) will be summarized for each active dosing regimen and its matching vehicle placebo in Table 14.1.2.

All subjects' demographic characteristics will be presented in Listing 16.2.4.1.

## 6.4. Significant Medical/Surgical History

Significant medical, surgical, ocular medical, and ocular surgical history will be coded using Medical Dictionary for regulatory Activities (MedDRA version 22.0 – March 2019) and will be summarized by system organ class (SOC) and by preferred term (PT) by each active dosing regimen and its matching vehicle placebo for the safety population in Table 14.1.3. All medical/surgical history will be presented in Listing 16.2.4.2.

## 6.5. Prior/concomitant/follow-up medications (including dictionary)

Prior/concomitant/follow-up medications, including rescue medications, will be coded using World Health Organization (WHO) Drug Dictionary WHODRUG B3 GLOBAL (MARCH 2019) and will be summarized by medication class and medication name presented for each active dosing regimen and its matching vehicle placebo group for the safety population in Table 14.1.5.

All prior/concomitant/follow-up medications will be presented in Listing 16.2.9.1.

## 6.6. Changes to Protocol-Planned Analyses

- Added analyses for ACC grade at PODs 4, 8, 15 (and 22 for Part A).

## 6.7. Appendix A: ABBREVIATIONS

| Abbreviation | Definition |
|---|---|
| ACC | Anterior Chamber Cell |
| ACF | Anterior Chamber Flare |
| AE | Adverse Event |
| ALP | Alkaline Phosphatase |
| ALT | Alanine Amino Transferase |
| AST | Aspartate Amino Transferase |
| BCVA | Best Corrected Visual Acuity |
| BID | Twice Daily |
| BSL | Baseline |
| BUN | Blood Urea Nitrogen |
| CFB | Change from Baseline |
| CI | Confidence Interval |
| ConMed | Concomitant Medications |
| CSR | Clinical Study Report |
| EOT | End of Treatment |
| EOS | End of Screening |
| IOP | Intraocular Pressure |
| ITT | Intent-to-Treat |
| MCH | Mean Corpuscular Hemoglobin |
| MCHC | Mean Corpuscular Hemoglobin Concentration |
| MCV | Mean Corpuscular Volume |
| MedDRA | Medical Dictionary for Regulatory Activities |
| OD | Right Eye |
| OS | Left Eye |
| OU | Both Eyes |
| PP | Per Protocol |
| QD | Once Daily |
| RBC | Red Blood Cell |
| SAP | Statistical Analysis Plan |
| SD | Standard Deviation |
| WHO | World Health Organization |

## 6.8. Appendix B: Clinical Laboratory Parameters

**Part A ONLY**: Clinical chemistry and hematology parameters. Venous blood samples are drawn at POD1 (pre-dose of study drug), POD22 (or EOT visit) and at the EOS visit.

If a subject is rescued prior to POD22, then the venous blood samples are drawn on the day that the subject discontinues the study drug (EOT), or as soon as possible after that. All rescued subjects have another blood draw at EOS visit.

If a subject withdraws from study early (early termination), then the venous blood samples are drawn on the day that the subject discontinues the study drug (EOT). They do not have another blood test for EOS visit.

**Hematology**

| | |
|---|---|
| Platelet Count | *RBC Indices*: |
| RBC Count | MCV |
| Absolute WBC Count (absolute) and automated differential WBC count | MCH |
| Hemoglobin | MCHC |

**Clinical Chemistry**

| | | | |
|---|---|---|---|
| Glucose | Chloride | Sodium | ALT (alanine amino transferase) |
| Calcium | BUN (blood urea nitrogen) | Potassium | AST (aspartate amino transferase) |
| Albumin | Creatinine | $CO_2$ | Bilirubin |
| Total protein | ALP (alkaline phosphatase) | | |

Serum cortisol concentration - Blood drawn at POD1/pre-Randomization and at POD22/EOT in Part A.

## 6.9. Appendix C: Modifications for Part B according to Amendment 1 of the Protocol

Based on the Amendment 1 of the protocol, the treatment duration of the study in Part B is shortened by one week. Accordingly, EOT visit (VISITNUM = 70) is planned at POD15 and EOS visit (VISITNUM=80) is planned at POD22.

## 7. REFERENCES

ICH E3

SAP template:

https://transceleratebiopharmainc.com/assets/clinical-content-reuse-assets/

**Tables**

[redacted]

[redacted]

[redacted]

**Figures**

[redacted]

**Listings**

[redacted]

[redacted]

**STATISTICAL ANALYSIS PLAN Appendix**

**VERSION: 1** 1

**EFFECTIVE DATE:** July 3rd, 2020

| VERSION HISTORY | | | |
|---|---|---|---|
| **SAP Number** | **Version Number** | **Effective Date** | **Revision** (Principal change from previous version) |
| 001 | 1 | | Not applicable, new SAP |
| APP001 | 1 | | Appendix to SAP001 |

## APPROVALS

Prepared By: [redacted] Date: 10 August 2020

Name:

Title: Biostatistics Contractor

Approved By: [redacted] Date: 8 August 2020

Name:

Title: Chief Medical Officer

Approved [redacted] Date: 10 August 2020

Name:

Title: Chief Executive Officer

## Table of Contents

**Introduction**

The purpose of this statistical analysis plan (SAP) appendix is to describe the corrections and modifications to the SAP001.

1. **Corrections**

| Page | Original Version | New Version | Comments |
|---|---|---|---|
| 18 | Pain Grade "4: Moderate: Presence of moderate throbbing or aching pain leading to the desire to use an analgesic." | Pain Grade "4: Severe: Presence of severe throbbing or aching pain that is not tolerable" | Error |

2. **Modifications**

| Page | Original Version | Changes | Comments |
|---|---|---|---|
| 16 | "LOCF will not be used for "complete" subjects even if they have stopped study drug earlier than POD21 (Part A) and POD14 (Part B)." | Removed from SAP. | The change reflects the intended purpose of the LOCF analysis. |
| 21 | For **changes from baseline** of ACC count, ACC grade, pain grade, ACF grade, and ETDRS acuity (logMAR score), statistical comparison between each active dosing regimen and its matching vehicle | 1. The comparison was carried out for the **means** of the efficacy endpoints as well.<br>2. For efficacy endpoints, the Pearson-Chi-Square test was used to compare the proportions of | New Exploratory analyses added. |

| | | | |
|---|---|---|---|
| | placebo will be carried out for each visit during POD4 - POD22 (Part A) and POD4 – POD15 (Part B) using t-test and Mann-Whitney non-parametric tests. | "resolved" subjects ('Sustained' Grade = 0) between each active group and its matching placebo group at POD4 and sustained at all later visits.<br>3. IOP means and changes from baseline were compared between active treatment groups and there matching placebo groups. | |
| 21 | Sensitivity Analyses:<br>"A subset of efficacy analyses will be examined for the per-protocol population as supportive analysis." | These analyses will not be conducted. | Only 5 out of 132 (3.8%) subjects were excluded from Per Protocol population because of protocol deviations. The differences from the LOCF analyses of efficacy endpoints will be negligible. |
| 21 | Sensitivity Analyses:<br>"Since only first ACC count will be used to define the proportion of subject with ACC count = 0, | These analyses will not be conducted. | The analyses will use the first ACC count - this is comparable to real-world clinical practice. Because only 6 (4.5%) subjects had |

| | | | |
|---|---|---|---|
| | analyses of using second ACC count and/or a combination of the two counts will be explored." | | different ACC counts at a visit, the other analyses are redundant. |
| | | 'Surgical Medications' are defined as routine medications related to cataract surgery that are used from 7 days before surgery to 1 day after surgery in this study. | New definition to distinguish the use of medications for the cataract surgery in this study from the use related to prior ocular surgery. |