APPENDICES

16.1 STUDY INFORMATION

16.1.9 DOCUMENTATION OF STATISTICAL METHODS

CLARA_SAP_V1_14Nov2024

CLARA: A Phase 1/2 Multi-center, Randomized, Double-Masked, Prospective, Parallel- Arm Study of AURN001 in Subjects with Corneal Edema Secondary to Corneal Endothelial Dysfunction (ABA-1

Statistical Analysis Plan

for Protocol: ABA-1

Version: 1.0

Version Date: 14-Nov-2024

Sponsor
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SAP APPROVAL – SIGNATORY

Study ID: ABA-1

Study Title: CLARA: A Phase 1/2 Multi-center, Randomized, Double-Masked, Prospective, Parallel- Arm Study of AURN001 in Subjects with Corneal Edema Secondary to Corneal Endothelial Dysfunction (ABA-1)

SAP Version: V1.0, 13-Nov-2024

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1 LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Term	Definition
AE	Adverse Event/Experience
AURN001	*Neltependocel* and Y-27632
[redacted]	[redacted]
BCVA	Best Corrected Visual Acuity
CEC	Corneal Endothelial Cells
CFB	Change from Baseline
CI	Confidence Interval
CRF	Case Report Form
[redacted]	[redacted]
ETDRS	Early Treatment of Diabetic Retinopathy Study
FAS	Full Analysis Set
FDA	Food and Drug Administration
GCP	Good Clinical Practice
ICH	International Council on Harmonization
IOP	Intraocular Pressure
IP	Investigational Product
[redacted]	[redacted]
LogMAR	Logarithm of the Minimum Angle of Resolution
neltependocel	Allogeneic human corneal endothelial cells
OCT	Optical Coherence Tomography
OD	Oculus Dexter or Right Eye
OS	Oculus Sinister or Left Eye
PPS	Per Protocol Set
PRO	Patient Reported Outcomes
SD-OCT	Spectral Domain Optical Coherence Tomography
SAE	Serious Adverse Event/Experience
TEAE	Treatment Emergent Adverse Event
UCVA	Uncorrected Visual Acuity
UPT	Urine Pregnancy Test
US	United States
VA	Visual Acuity
[redacted]	[redacted]
WOCBP	Women of Childbearing Potential
Y-27632	A Rho-kinase inhibitor small molecule drug

2 INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to describe the planned analyses and reporting for protocol ABA-1, Version 5.0, dated the 04-Jun-2024.

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

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

3 TRIAL OBJECTIVES

The primary objective of this trial is to evaluate:

- Efficacy of a single injection of different concentrations of *neltependocel* in combination with Y-27632 (i.e., AURN001), *neltependocel* alone, and Y-27632 alone in subjects with corneal edema secondary to corneal endothelial dysfunction

The secondary objective of this trial is to evaluate:

- Safety and tolerability of a single injection of different concentrations of *neltependocel* in combination with Y-27632 (i.e., AURN001), *neltependocel* alone, and Y-27632 alone in subjects with corneal edema secondary to corneal endothelial dysfunction

4 TRIAL DESIGN

4.1 Description of Trial

This is a multicenter, randomized, double-masked, parallel-arm, dose-ranging, Phase 1/2 study of AURN001 in subjects with corneal edema secondary to corneal endothelial dysfunction. The efficacy and safety of AURN001 will be assessed in a clinical trial setting in North America in adult subjects with corneal edema secondary to corneal endothelial dysfunction. Three doses of AURN001 compared with the 2 components of AURN001 separately (*neltependocel* and Y-27632) will be evaluated to assess the contribution of these 2 elements to the efficacy and safety of AURN001.

This trial will enroll approximately 100 subjects in the 5 treatment arms with approximately 20 subjects per arm. A randomized treatment sequence will be assigned. The sponsor will assess the actual enrollment in each arm on an on-going basis throughout the study to maintain a

randomization ratio of 1:1:1:1:1. The sponsor will make adjustments to the randomized treatment sequence and the number of subjects to be treated in each cohort as needed.

The treatment arms are as follows:

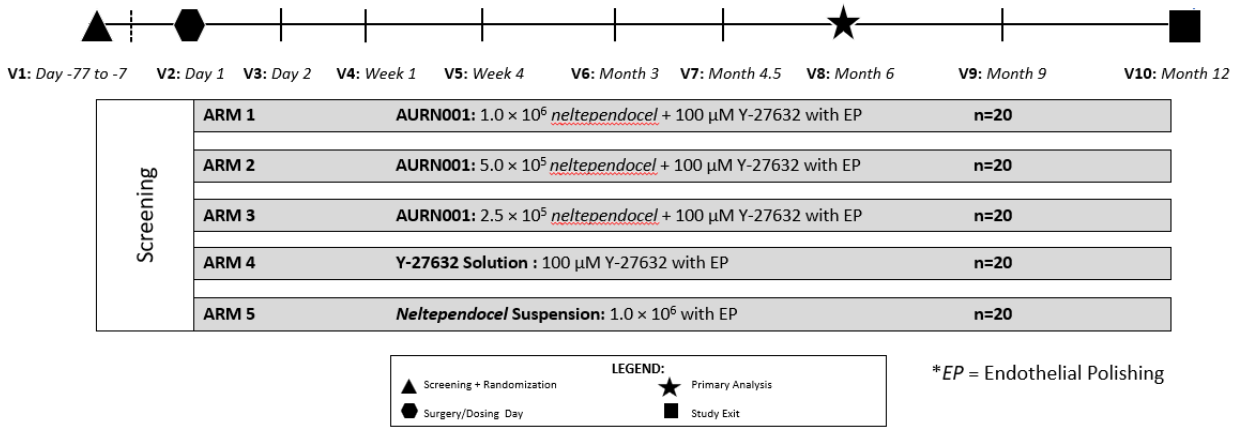
Table 1 Treatment Assignment Paradigm

Arm	No. of Subjects	*Neltependocel* Dose	Y-27632 Dose	Endothelial Polishing?
1	20	1.0×10^6	100 µM	Yes
2	20	5.0×10^5	100 µM	Yes
3	20	2.5×10^5	100 µM	Yes
4	20	None	100 µM	Yes
5	20	1.0×10^6	None	Yes

This study will have a screening period, a surgery/treatment day during which treatment will be administered, and a 12-month observation period. The primary efficacy analysis will be conducted at Month 6. The study will have up to 10 visits with one optional visit: the Screening Visit (Visit 1, -77 days to -7 days); Surgery/Treatment (Visit 2, Day 1); and Follow-up (Visits 3 through 10, Day 2, Week 1, Week 4, and Months 2 (optional), 3, 4.5, 6, 9, and 12, respectively). Unscheduled visits will be allowed, as deemed necessary by the investigator.

This study will be conducted per the schedule shown in Figure 1.

Figure 1 Study Schematic



Assessments can be found in the Schedule of Assessments in Appendix 1.

4.2 Study Endpoints

4.2.1 Efficacy Endpoints

All ocular assessments will be conducted on both eyes. The efficacy evaluations will be based on measurements of BCVA (using ETDRS), ultrasonic contact pachymetry, [redacted]

4.2.1.1 Primary Efficacy Endpoints

- Response, defined as a ≥15-letter improvement (3-line gain) from baseline in best-corrected visual acuity (BCVA) at Month 6

4.2.1.2 Secondary Efficacy Endpoints

- Change from baseline in BCVA at Month 6
- Change from baseline in central corneal thickness (CCT) at Month 6
- Response, defined as a ≥15-letter improvement (3-line gain) from baseline in BCVA at all other timepoints
- Change from baseline in BCVA at all other timepoints
- Change from baseline in CCT at all other timepoints
- Response, defined as a ≥10-letter improvement (2-line gain) from baseline in BCVA at each timepoint

[redacted]

4.2.2 Safety Evaluations

- Incidence and severity of ocular treatment-emergent adverse events (TEAEs)
- Incidence and severity of non-ocular TEAEs
- Loss from baseline in BCVA ≥15 letters
- Rescue rate and time to rescue

- Graft rejection

The safety evaluations will be based on adverse event (AE) reporting, laboratory findings (clinical chemistry and hematology), and ophthalmic examinations, including Goldmann tonometry, Slit Lamp biomicroscopy, gonioscopy, dilated fundoscopy, and BCVA (as measured by ETDRS).

4.3 Randomization and Masking

This study will be double-masked and will utilize a randomized treatment sequence model. A computer-generated encrypted read-only randomized treatment sequence schedule will be provided by a biostatistician. The randomized treatment sequence schedule will be managed by unmasked team members responsible for assessing enrollment in each arm to maintain a randomization ratio of 1:1:1:1:1.

4.4 Trial Treatment

Subjects eligible to be treated will receive a single injection of AURN001 (*neltependocel* with Y-27632), *neltependocel* alone, or Y-27632 alone into the anterior chamber of the study eye. The dose of *neltependocel* will be either 1.0×10^6, 5.0×10^5 or 2.5×10^5 cells; the dose of Y-27632 will be 100 µM. The total volume of administration will be approximately 300 µL.

The injection of study treatment into the study eye will be performed under local anesthesia (administration method at the investigator's discretion). After creating a small incision at the corneal limbus, the corneal endothelium will be polished to a diameter of approximately 8 mm. Study treatment will be injected into the anterior chamber using a 27-gauge needle. Immediately after completion of surgery, subjects will lie face down for approximately 3 hours (±15 minutes).

For detailed instructions, please refer to the Procedure Manual, which includes sponsor observation language.

5 ANALYSIS SETS

5.1 Full Analysis Set

The Full Analysis Set (FAS) will be defined as all randomized subjects who received any amount of study drug during intracameral injection. All subjects in FAS will be analyzed according to the treatment they actually received. The Full Analysis Set will be the primary population for evaluating all efficacy endpoints, subject characteristics, and protocol deviations.

5.2 Per Protocol Set

Per Protocol Set (PPS) will be a subset of FAS, excluding subjects who have major protocol deviations, which impact the primary endpoint evaluation. The per protocol set will be used for the sensitivity analyses of the primary endpoint.

5.3 Safety Analysis Set

The Safety Analysis Set will be the same as FAS. The safety analysis set will be the primary population for evaluating treatment administration, concomitant medication and safety.

6 GENERAL CONSIDERATIONS

6.1 Data Analysis Conventions

Statistical programming and analyses will be performed using SAS® Version 9.4 or higher.

Summaries for continuous and ordinal variables will include the number of observations (n), arithmetic mean, standard deviation (SD), median, minimum, and maximum. Minima and maxima will be reported with the same precision as the raw values; means and medians will be presented to one additional decimal place than reported in the raw values. Standard deviations will be presented to two additional decimal places than reported in the raw values.

Summaries for discrete variables will include counts and percentages. All percentages will be rounded to one decimal place.

All safety and efficacy summaries will be presented by treatment group and overall, where appropriate, for each study visit. Listings will be sorted by treatment group, subject number, study visit, and parameter, as applicable.

6.2 Treatment Comparison

For the purpose of statistical comparison, each combination arm will be compared to each component. That is the 3 different concentrations of *neltependocel* in combination with Y-27632 (i.e., AURN001) will be compared to *neltependocel* alone, and to Y-27632 alone.

Two components will also be compared to each other. That is *neltependocel* alone compared to Y-27632 alone.

6.3 Definition of Baseline

Baseline measurements are the last measurement prior to the study drug injection on Day 1. Change from baseline values will be calculated as follow-up visit minus baseline visit.

6.4 Definition of Study Day

Start day of study treatment is the day of the first dose of study treatment, i.e. Day 1 as defined in the protocol.

The study day for assessments occurring on or after the start of study treatment (e.g., adverse event onset) will be calculated as:

Study day = Date of the assessment/event - start date of study treatment + 1.

The study day for assessments occurring prior to the first dose of study treatment (e.g., medical history) will be negative and calculated as:

Study day = Date of the assessment/event - start date of study treatment.

The study day will be displayed in all relevant data listings.

6.5 Unscheduled visits

All by-visit assessments will be summarized and presented using the nominal visit provided in the data. Programmatic visit windows will not be used, unless otherwise specified.

Unscheduled visits will be used in the determination of baseline. All data, including unscheduled visits, will be present in data listings.

7 STATISTICAL METHODS

7.1 Study Reporting

There will be two reporting events for this study, one reporting when all subjects complete Month 6 visit and another reporting when all subjects complete the study (Month 12 visit). For the first reporting, when all subjects complete the Month 6 visit, data will be cleaned and frozen at the subject visit level. The sponsor will be unmasked for the 6 months efficacy and safety analyses. AE starting after the Month 6 visit will not be included for Month 6 reporting for better risk-benefit assessment. All other data after Month 6 visit will be included and reported as they are. For the second data reporting, when all subjects complete the entire 12-month study, data will be cleaned, and the database will be locked.

7.2 Unit of Analysis

The unit of analysis in this study will be the study eye for all efficacy and ocular safety summaries. Additionally, non-ocular adverse events (AEs) and medical history will be presented at the subject level.

The non-study eye safety summaries will also be presented as appropriate.

7.3 Sample Size Determination

This study is not powered to show statistical significance but will provide initial estimates and trends of the endpoints for use in future trial designs. The sample size will allow for safety information to be obtained, while still limiting the number of subjects exposed to the IP. Statistical analysis will be descriptive.

7.4 Statistical Significance

All statistical testing will be done at the two-sided alpha level of 0.05. As this is a Phase 1/2 study, no adjustments to alpha will be made for the tests of multiple comparisons and multiple endpoints. Statistical analysis will be descriptive.

7.5 Interim Analysis

As stated in Section 7.1, there will be an interim reporting when all subjects complete the primary endpoint at Month 6. As this analysis is for all subjects completing the primary endpoint, this analysis is considered the study primary efficacy analyses. And hence, there will not be alpha adjustment. All p-values will be judged at 2-sided alpha level of 0.05. All p-values are considered nominal.

7.6 Statistical Hypothesis

This is a Phase 1/2 study. No formal statistical hypothesis is considered.

7.7 Adjustments for Multiplicity

[redacted]

7.8 Adjustment for Covariates

Change from baseline in BCVA and CCT at Month 6 will be analyzed using Analysis of covariance (ANCOVA) for the full analysis set. Baseline of BCVA and CCT will be used as covariate for the adjustment.

7.9 Handling of Data after Rescue

For this study reporting, any data collected at and after rescue visits will not be used for the analyses and summary tables but will be included in the listings. This applies to both efficacy and safety tables as well as concomitant medication tables. The only exception is that adverse events collected at and after rescue visits will be summarized separately as described in Section 14.1.

7.10 Missing Data Imputation for Efficacy Endpoints

The study primary endpoint is proportion of subjects having a ≥15-letter improvement (3-line gain) from baseline in best-corrected visual acuity (BCVA) at Month 6. For the primary analysis, intercurrent events will be addressed using composite variable strategies. That is subjects who received any rescue surgeries prior to Month 6 or drop out the study due to any reasons prior to Month 6 will be imputed as treatment failure (i.e. not improve by >= 15 letters).

For the statistical analysis, the following two binary endpoints will be imputed using the same method as the primary endpoint:

- proportion of subjects having a ≥10-letter improvement (2-line gain) from baseline in best-corrected visual acuity (BCVA) at Month 6
- [redacted]

In addition, the following two continuous endpoints will be imputed using last observation carried forward (LOCF) for their statistical analyses:

- best-corrected visual acuity (BCVA)
- central corneal thickness (CCT)

7.11 Partial or Missing Date Handling

Partial or missing dates will be imputed when complete dates are required to flag data as treatment-emergent or concomitant with treatment.

Partial/missing start and end dates for AEs and concomitant medications will be imputed as follows.

Partial/missing start date:

- Dates with missing day only will be imputed as the 1st of the month unless the month and year are same as the month and year of first dose of study medication, in which case missing day will be imputed as the first dose day of study medication.
- Dates with both day and month missing will be imputed as 1 Jan unless the year is same as the year of first dose of study medication, in which case missing day and month will be imputed as the first dose day and month of study medication.
- Completely missing dates will be imputed as the first dose date of study medication unless the end date is on or before the first dose date of study medication, in which case missing date will be imputed as 1 Jan of the same year as the end date.

Partial/missing end date:

- Dates with missing day only will be imputed as the last day of the month.
- Dates with both day and month missing will be imputed as 31 Dec.
- If the ongoing flag is missing or “Yes” then the date will not be imputed unless death date is available, in which case the missing date will be imputed as the death date. If ongoing is “No” then the missing end date will be imputed as the last dose date.
- If the imputed date is after the date of death, then the end date will be set equal to the date of death.
- The original dates will be displayed in data listings and the imputed dates will be used in derivations only (study day, treatment-emergence status, etc.).

7.12 Subpopulations

Not applicable.

8 SUBJECT DISPOSITION

Subject disposition will be summarized by treatment group and overall.

The disposition table will include the numbers of subjects

- who were screened, screened but not randomized, randomized, and randomized but not treated,
- in full analysis set, in per-protocol set, and in safety analysis set.
- discontinued the study prior to Month 6,
- discontinued the study and completed the study.

The percentages will be calculated using the number of subjects from the full analysis set as the denominator, unless otherwise noted. Reasons for study discontinuation will be summarized. Inclusion and exclusion criteria not met for screening failure subjects will also be summarized.

Subject disposition data will be presented in a listing.

9 PROTOCOL DEVIATIONS

Protocol deviation will be reviewed by the sponsor at on-going basis. The deviation file will include a description of the protocol deviations, as well as classification of major or minor. Major deviations will further be categorized by different deviation categories. Number and percentage of subjects with major protocol deviations will be summarized by deviation category. For the protocol deviation summaries, any data collected at and after rescue visits will not be used.

Protocol deviations, including both major and minor deviations, will be presented in a listing.

The final criteria for the per-protocol set, regarding which protocol deviations that warrant exclusion, will be determined during the blinded data review when all data on protocol deviations are available and before breaking the blind.

10 DEMOGRAPHIC AND BASELINE CHARACTERISTICS

10.1 Demographics

The demographic variables collected in this study include age, gender, ethnicity, and race.

Age (years) will be summarized using descriptive statistics as a continuous variable. Age group (< 65 years, ≥ 65 years) gender, ethnicity, and race will be summarized using counts and percentages.

Demographic characteristics will be presented in a listing.

10.2 Baseline Characteristics

Baseline characteristics will be summarized for study eye and non-study eye separately.

The following baseline characteristics will be summarized:

- BCVA (ETDRS)

- Central corneal thickness (CCT)
- [redacted]
- [redacted]

The subject baseline characteristics will be presented in a listing.

In addition, screening BCVA will be summarized for study eye and non-study eye separately.

- Number of subjects with BCVA < 65 letters and ≥ 65 letters

11 MEDICAL HISTORY AND MEDICATIONS

11.1 Medical History

Ocular and non-ocular medical history will be coded using Medical Dictionary for Regulatory Activities (MedDRA) version 26.1 and summarized by system organ class (SOC) and preferred term (PT). Subjects are counted only once under each SOC or PT for which they have at least one medical history.

Ocular medical history will be summarized using discrete summary statistics and presented separately for study eye and non-study eye. Non-ocular medical history will be similarly summarized but at the subject level.

Subject medical history data will be presented in separate listings for ocular and non-ocular data.

11.2 Prior and Concomitant Medications

Prior and concomitant medications will be coded using the World Health Organization Drug Dictionary (WHODRUG) GLOBAL B3 September 1, 2023 and summarized by therapeutic drug class (Anatomical Therapeutic Chemical [ATC] 3 classification) and preferred name. Subjects are counted only once under each therapeutic class or preferred name (generic drug name) for which they have at least one concomitant medication. If the ATC3 classification is not provided, then the next lowest classification that is provided in the coding dictionary will be used.

Concomitant medications are medications which started 1) prior to initiation of study treatment administration and continuing for any period of time following the Day 1 administration of study treatment or 2) at any time following the Day 1 administration of study treatment. Prior medications are medications which are started before the Day 1 administration of study drug.

Ocular prior and concomitant medications will be summarized using discrete summary statistics and presented separately for study eye and non-study eye. Non-ocular prior and concomitant medications will be similarly summarized but at the subject level. For the concomitant summaries, any data collected at and after rescue visits will not be used.

Subject concomitant medications will be presented in separate listings for ocular and non-ocular data. The listings will indicate if medications are prior and/or concomitant medications.

12 TREATMENT EXPOSURE AND NUMBER OF INJECTIONS

12.1 Study Injection Summary

The number of subjects receiving study injections in the Study Eye on Day 1 visit will be summarized with count and percentage by treatment group. Exposure data will be presented in listings.

13 EFFICACY ANALYSES

13.1 Primary Efficacy Endpoint

The study primary efficacy endpoint is the proportion of subject having a ≥15-letter improvement (3-line gain) from baseline in best-corrected visual acuity (BCVA) at Month 6.

13.1.1 Primary Analysis

For the primary endpoint analysis, number and percentage of responders, with associated 2-sided exact (Clopper-Pearson) 95% confidence intervals (CIs), will be presented by treatment group. Proportion of responders will be companied between treatment groups using a two-sided Fisher's exact test. As stated in Section 7.10, subjects who received any rescue surgeries prior to Month 6 or drop out the study due to any reasons prior to Month 6 or missing data at Month 6 will be imputed as treatment failure (i.e. not improve by >= 15 letters).

13.1.2 Sensitivity Analyses

A completer analysis will be performed. That is the primary analysis will be repeated for subjects who complete Month 6 visit, i.e. analysis based on the observed data. Any data collected at and after rescue visits will not be used. The primary analysis will also be repeated based on per protocol set.

13.2 Secondary Efficacy Endpoints

Change from baseline in BCVA and CCT at Month 6 will be analyzed using Analysis of covariance (ANCOVA) for the full analysis set. The model will include treatment arm as a categorical variable and baseline as a covariate. Treatment comparison of BCVA and CCT at Month 6 will be conducted. Point estimates, 95% confidence intervals and p-values will be provided. Any data collected at and after rescue visits will not be used. As stated in Section 7.10, LOCF will be used to impute the missing values.

Proportion of subjects having ≥10-letter improvement (2-line gain) from baseline in BCVA at Month 6 will be analyzed using the same method as the analyses of the primary endpoint. For this analysis, missing data will be imputed using the same method as the primary endpoint.

Descriptive summary statistics will be provided for all the secondary endpoints listed in Section 4.2.1.2. Any data collected at and after rescue visits will not be used.

In addition, 3, 2, and 1-ine gain and 3, 2, and 1-line loss in BCVA will be summarized by dose and visit. Change from baseline within 10 letters (<10 letters gain and <10 letters loss) will be labeled as 0-line and will also be part of the summary. Summaries will include count, percentage and cumulative percentages. Any data collected at and after rescue visits will not be used.

Change from baseline in BCVA and CCT will also be summarized descriptively using LOCF imputation. Any data collected at and after rescue visits will not be used.

[redacted]

14 SAFETY ANALYSES

14.1 Adverse Events

Adverse events will be coded using Medical Dictionary for Regulatory Activities (MedDRA) version 26.1.

Treatment-emergent adverse events (TEAEs) are defined as any adverse events that occur during or after the Day 1 injections, or any adverse events that are continuous from the screening but worsen during or after the Day 1 injections.

Ocular and non-ocular TEAEs will be summarized separately. Summary of ocular TEAEs will be separated by study eye and non-study eye.

An overall summary including the number of events and the number and percentage of subjects who experienced at least one TEAE will be presented by treatment group and overall. The overall summary will also include at least one serious TEAE, treatment-related TEAE, treatment-related serious TEAE, TEAE leading to subject discontinuation from the study, and TEAE leading to death.

TEAEs will be summarized by System Organ Class (SOC) and Preferred Term (PT). Subjects are counted only once under each SOC or PT for which they have at least one TEAE. Summaries by relationship to study product, by relationship to study procedure and by maximum severity will also be provided.

Serious TEAEs will not be summarized in table format as it is anticipated number of serious TEAEs will be very limited.

In addition, the following AE summaries will be provided for AEs collected at and after rescue visits:

- Overall summary of TEAE
- TEAE by SOC and PT

For these summaries, denominators to be used for percentage calculation will be number of Rescued subjects.

All AEs will be presented in a subject listing with a flag indicating TEAE and a flag indicating AEs occurred at and after rescue visits. In addition, all serious AEs will be presented in a separate listing.

14.2 Vision Loss

The number and percentage of subjects who have loss from baseline in BCVA ≥15 letters will be summarized using counts and percentages at each post-baseline visit by treatment group and overall.

The best corrected visual acuity will be presented in a listing.

14.3 Rescue Surgery

Rescue surgeries include rescue surgeries given by the investigators even when the rescue criteria were not met.

The number of rescue surgeries will be summarized descriptively by visit. Use of rescue surgeries will be presented in a listing.

Time to rescue surgery is defined as the time duration from Day 1 to rescue date plus 1 for rescue subjects, and from Day 1 to last visit plus 1 for non-rescue subjects.

Medians with 95% CI of time to rescue surgery will be provided and Kaplan-Meier plots will be produced. Time to rescue surgery will be presented in a listing.

14.4 Graft Rejection

The Clinical study report will discuss any cases of graft rejection if there are any.

14.5 Slit-lamp Examination

Slit-lamp examination data will be summarized by visit and by eye, and a subject listing will be presented.

14.6 Gonioscopy

Gonioscopy data will be summarized by visit and by eye, and a subject listing will be presented.

14.7 Dilated Fundus Ophthalmoscopy

Dilated fundus ophthalmoscopy data will be summary by visit and by eye, and a subject listing will be presented.

14.8 Spectral Domain Optical Coherence Tomography

Spectral Domain Optical Coherence Tomography (SD-OCT) macula data will be summarized by visit and by eye, and a subject listing will be presented.

14.9 Intraocular Pressure

The observed and change from Baseline in IOP will be summarized for study eye and non-study eye separately using continuous descriptive statistics at each post-baseline visit by treatment group and overall.

The number and percent of subjects with a ≥ 10 mmHg increase from baseline and the number and percent of subjects with a ≥ 30 mmHg observed value will be presented.

Post-baseline IOP data will be presented in a listing, along with flags indicating a ≥ 10 mmHg increase from baseline and a ≥ 30 mmHg observed value.

IOP data will be presented in a listing.

14.10 Clinical Laboratory Data

Clinical laboratory testing will include clinical chemistry and hematology evaluations. The quantitative variables and change from baseline will be summarized by treatment group and overall by study visit using continuous descriptive statistics. The counts and percentages of qualitative variables will be summarized by treatment group and overall by study visit.

Clinical laboratory results will be presented in a listing.

14.11 Urine Pregnancy Test

Urine pregnancy tests will be presented in a listing.

15 CHANGES FROM PROTOCOL-STATED ANALYSES

There are no changes to the protocol-stated analyses.

16 REVISION HISTORY

Documentation of revision to the SAP will commence after approval of Final version 1.0.

Appendix 1 Schedule of Assessments

Study Period	Screening Visit	Observation Period										
		Day 1/ Procedure	Day 2	Week 1	Week 4	Month 2 (optional)	Month 3	Month 4.5	Month 6	Month 9	Month 12 / Study Exit	Un-scheduled Visit
Visit Number	**1**	**2**	**3**	**4**	**5**	**5.1**	**6**	**7**	**8**	**9**	**10**	
Study Day (D) or Week (W)/ Visit Window	**-77 to -7**	**D1**	**D2 (+2d)**	**D8 (+2d)**	**D30 (±7d)**	**D60 (±7d)**	**D90 (±7d)**	**D135 (±14d)**	**D180 (±14d)**	**D270 (±14d)**	**D360 (±14d)**	**N/A**
Informed Consent	X											
Demographics	X											
Medical/Surgical History	X											
Eligibility Review	X											
Cohort Assignment	X											
Surgery/Study Treatment		X										
Ophthalmic Assessments (To be Conducted in Both Eyes)												
UCVA [a]	X		X	X	X	X	X		X		X	(x)
BCVA (ETDRS) by MR (through phoropter) [a]	X				X	X	X	X	X	X	X	(x)
[redacted]												
SD-OCT (Macula)	X						X		X		X	(x)
CCT by Ultrasonic Contact Pachymetry	X			X	X	X	X	X	X	X	X	(x)
Slit Lamp Biomicroscopy	X		X	X	X	X	X	X	X	X	X	(x)
Slit Lamp Photography	X				X	X	X		X	X	X	(x)
Goldmann Tonometry (IOP)	X		X	X	X	X	X	X	X	X	X	(x)
Gonioscopy	X						X		X		X	(x)
Dilated Fundus Examination	X						X		X		X	(x)

Study Period	Screening Visit	Observation Period										
		Day 1/ Procedure	Day 2	Week 1	Week 4	Month 2 (optional)	Month 3	Month 4.5	Month 6	Month 9	Month 12 / Study Exit	Un-scheduled Visit
Visit Number	**1**	**2**	**3**	**4**	**5**	**5.1**	**6**	**7**	**8**	**9**	**10**	
Study Day (D) or Week (W)/ Visit Window	**-77 to -7**	**D1**	**D2 (+2d)**	**D8 (+2d)**	**D30 (±7d)**	**D60 (±7d)**	**D90 (±7d)**	**D135 (±14d)**	**D180 (±14d)**	**D270 (±14d)**	**D360 (±14d)**	**N/A**
Other Assessments												
Adverse Events		X	X	X	X	X	X	X	X	X	X	X
Prior/Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X
[redacted]												
Laboratory blood draw (hematology, chemistry)	X								X		X	
Urine Pregnancy[b]	X	X----------									----------X	(x)

[redacted] BCVA = best-corrected visual acuity; ETDRS = Early Treatment of Diabetic Retinopathy Study; MR = manifest refraction; IOP = intraocular pressure; N/A = not applicable;; PRO = patient reported outcome; SD-OCT = spectral domain-optical coherence tomography; (x) = optional (at the discretion of the investigator); UCVA = uncorrected visual acuity; VA = visual acuity; [redacted]

[redacted]

[b.] For women of childbearing potential, a urine pregnancy test is to be conducted at the Screening Visit. Thereafter, if the subject misses 2 consecutive menstrual cycles, a urine pregnancy test is to be conducted and followed by a serum pregnancy test if the urine test is positive.