VegaVect, Inc.

Protocol: 15-EI-0038

Study Title:

A Phase I/IIa Study of RS1 Ocular Gene Transfer for X-linked Retinoschisis (XLRS2)

Statistical Analysis Plan

Version 1.0, September 6, 2024

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STUDY INFORMATION

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VERSION HISTORY

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SIGNATURE PAGE

[redacted]

LIST OF ABBREVIATIONS

AAV	Adeno-associated Virus
AC	Anterior Chamber
AIC	Akaike information criterion
ATC	Anatomical Therapeutic Chemical
AE	Adverse Event
b/a	b-wave/a-wave ratio
BCVA	Best-Corrected Visual Acuity
CI	Confidence Interval
CTCAE	Common Terminology Criteria for Adverse Events
DM	Diabetes Mellitus
DSMC	Data and Safety Monitoring Committee
EDC	Electronic Data Capture
EMR	Medical Record System
ERG	Electroretinography
ETDRS	Early Treatment Diabetic Retinopathy Study
EVA	Electronic Visual Acuity
FDA	Food and Drug Administration
HIV	Human Immunodeficiency Virus
ICH	International Conference on Harmonisation
IOP	Intraocular Pressure
IP	Investigational Product
IRB	Institutional Review Board
LLVA	Low Luminance Visual Acuity
logMAR	Logarithm of the Minimum Angle of Resolution
MedDRA	Medical Dictionary for Regulatory Activities
NEI	National Eye Institute
NIH	National Institutes of Health
OCT	Optical Coherence Tomography
PT	Preferred Term
RSI	Retinoschisin
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SD	Standard Deviation
SOC	System Organ Class
VA	Visual Acuity
WHO	World Health Organization
XLRS	X-linked Retinoschisis

1 INTRODUCTION

1.1 Purpose and Structure of the Document

This Statistical Analysis Plan (SAP) provides proposed analyses for the study "A Phase I/IIa Study of *RS1* Ocular Gene Transfer for X-linked Retinoschisis (XLRS2)."

This document describes all planned analyses and provides reasons and justifications for these analyses. It also includes sample tables, listings, and figures planned for the final analyses. Regarding the final analyses and Clinical Study Report (CSR), this SAP follows the International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use Guidelines, as indicated in Topic E3 (Structure and Content of Clinical Study Reports), and more generally is consistent with Topic E8 (General Considerations for Clinical Trials) and Topic E9 (Statistical Principles for Clinical Trials). The structure and content of the SAP provides sufficient detail to meet the requirements identified by the Food and Drug Administration (FDA) and ICH, while all work planned and reported for this SAP will follow internationally accepted guidelines published by the American Statistical Association and the Royal Statistical Society for statistical practice.

This document contains five broad sections: (1) a description of the purpose and timing(s) of analyses; (2) a description of the study design, its objectives; and the variables collected/assessed to be used in analyses; (3) general statistical principles; (4) comprehensive statistical analysis methods for study outcomes, and (5) a list of proposed tables, figures, and listings along with mock-ups (Appendices 1, 2, and 3). Any deviation from this statistical plan will be described and justified in protocol amendments and/or in the final study report, as appropriate.

1.2 Purpose of the Analyses

The final analyses will be performed after study completion, when all study data have been entered, all data queries have been resolved, and the database has been locked. These analyses will assess the safety and tolerability of a single intravitral administration of AAV8-scRS/IRBPhRS to the retina of participants affected with X-linked juvenile retinoschisis (XLRS).

2 INVESTIGATIONAL PLAN

2.1 Overall Study Design and Plan

The XLRS2 study is a Phase I/IIa, prospective, single-center, dose escalation study to evaluate the safety of AAV8-scRS/IRBPhRS gene (henceforth referred to as "AAV") transfer vector in up to 24 male participants with X-linked Retinoschisis (XLRS). The treated eye will be unmasked. Only one eye, the study eye, will be treated per participant. Data for untreated eyes will be collected for each of the study visits to serve as an untreated control to the study eye and to gather data on the natural history of human XLRS. Study eye eligibility criteria are described in Section 3.2 of the protocol. The study is unmasked and not randomized.

Upon consent and enrollment into the study, baseline testing was performed (Baseline 1) up to 90 days prior to the AAV vector injection, at which time the study eye was identified based on study eye eligibility criteria as outlined in Section 3.2 of the protocol. Two additional baseline visits occurred up to 60 days prior to AAV vector injection (Baseline 2), and on the same day as AAV vector injection or up to two days prior to AAV vector injection (Baseline 3). Medical and ophthalmic history, physical examinations, and testing with regards to syphilis, tuberculosis, hemoglobin A1C, HIV, Hepatitis B, and Hepatitis C were performed only at the Baseline 1 or Baseline 2 visit. AAV vector injection occurred at Day 0 with follow-up evaluations occurring

on Day 1, Day 7, Day 14, Month 1, Month 2, Month 3, Month 4, Month 6, Month 9, Month 12, and Month 18. Annual safety visits were performed starting at Year 2. Prior to Amendment X of the protocol (IRB approved March 24, 2022), annual safety visits were performed from Year 2 to Year 15. As of Amendment X, participant follow-up concluded at Year 5. Participants underwent medical evaluations, ophthalmic examinations, and visual function measurements at each scheduled visit (**Table 1**). Laboratory tests were performed through Month 18 and optionally at the annual safety follow-up visits.

If testing for a specified visit was not completed within a day, subsequent clinic visits may have been scheduled within the visit window to complete the scheduled evaluation. Additional visits may have been planned according to clinical need based upon the findings at each examination. Participants could choose to return to their community ophthalmologists between required study visits.

The dosing scheme included a maximum of six cohorts where dosing in the vector genomes ranged from 1e9 to a maximum of 6e11 (**Table 2).** The NEI independent Data and Safety Monitoring Committee (DSMC) reviewed cumulative data through Month 1 for each participant and each cohort. Following the review of the data, the NEI DSMC recommended enrolling additional participants in the current dose cohort or recommended dose modification. In addition, after a participant was dosed and there was one month of follow-up for each participant, the investigators and the DSMC reviewed the data to assess whether the immunomodulation regimen was appropriate. It was then decided, upon approval of the DSMC, whether additional participants may be injected, including possible modification of the immunomodulation regimen or dose. Amendment Y (IRB approved April 4, 2023) transferred data and safety monitoring purview from NEI's DSMC to VegaVect's Data and Monitoring Committee (DMC) Chair following protocol sponsor transfer from NEI to VegaVect.

At the time of finalization of v1.0 of the SAP, NEI was the only clinical site. The last participant last visit for the NEI site occurred on April 25, 2024. The protocol sponsor, VegaVect, intends to activate an additional site in the future. If an additional site is activated, the SAP will be updated and up versioned to appropriately account for the addition of the second site.

2.1.1. Suspension Rules

Occurrence of any of the following constituted grounds for suspending enrollment and investigational product (IP) administration to any further participants, pending NEI DSMC or VegaVect DMC Chair review as to continuing study enrollment:

1. A significant decrease in visual function (defined as a decrease in best-corrected visual acuity [BCVA] of ≥ 10 ETDRS letters; OR a decrease in electroretinography [ERG] response amplitude ≥ 75%) in the study eye, unless this decline is attributable to ocular surface effects or due to minimal inflammation (anterior chamber pigmented or nonpigmented cells of grade 1+ or less) from the intravitreal injection procedure during the first 10 days following IP administration;
2. Endophthalmitis in the study eye;
3. Anterior chamber cellular reaction of grade 3+ or higher in the study eye;
4. Vitreous cellular reaction of grade 3 or greater in any portion of the vitreous cavity in the study eye;
5. Optic nerve edema of grade 1+ or higher in the study eye;
6. Retinitis, retinal vasculitis or choroiditis in the study eye;
7. Systemic response as reflected by grade 2 laboratory tests or any grade 3-4 event/laboratory test that is related to the IP (grading according to the Common Terminology Criteria for Adverse Events [CTCAE] v5.0);
8. A suspected serious adverse reaction related to the study article.

2.2 Study Objectives and Outcomes

Objective:

- (Safety): To assess the safety and tolerability of a single intravitreal administration of AAV8-scRS/IRBPhRS.

Primary Outcome:

1. (Safety): Adverse events affecting ocular function that differ clinically from those expected in the normal course of progression of XLRS including:
    a. Substantial functional change as measured by a ≥ 10 EVA letters in BCVA (> 0.2 logMAR) from average of baseline 1 and 2 BCVA.
    b. Decrease in ERG response amplitude by ≥ 75% from average of amplitudes from baseline 1 and 2.
    c. Severe ocular inflammation beyond that inflammation anticipated consequent to an intravitreal injection.
    d. Adverse events deemed clinically related to the intraocular administration technique will also be noted and reported, including vitreous hemorrhage, retinal detachment, intraocular pressure elevation, lens damage and endophthalmitis.
    e. Abnormal findings of serum chemistry, hematology, liver function tests or urinalysis/urine chemistry that are beyond Grade 1 and/or clinically significantly different than baseline.

Secondary Outcomes:

- (Safety): Change in ERG combined response amplitudes from an average of Baseline 1 and 2 measurements and/or change in the b/a-wave amplitude ratio.
- (Safety): The mean, median and distribution of change in BCVA compared to the average of Baseline 1 and 2 measurements.
- (Safety): Changes in retinal structure as measured by OCT compared to the average of Baseline 1 and 2 measurements.
- (Safety): Change in central visual field sensitivity (i.e., mean sensitivities, number of scotomatous points, and number of points with a significant change in sensitivity) as measured by microperimetry (MP-1) Visual Field testing compared to the average of Baseline 1 and 2 measurements.

2.3 Study Flowsheet

The study flowsheet is presented in the protocol (**Appendix 1**) and is provided in the SAP for reference (**Table 1**).

2.4 Statistical Considerations for the Study Design

2.4.1 Sample Size Considerations

This study does not lend itself to a sample size calculation but has previously been discussed with the FDA who concurred with minimally three participants in each group. The protocol has been written according to this discussion. Subsequent protocol amendments provided for additional participants to be enrolled at doses

expected to be safe and potentially efficacious with concurrence of the DSMC. Total trial size is expected not to exceed 24 participants.

As of Modification Z (IRB approved September 26, 2023), NEI will conclude study enrollment with a total of 12 participants. Participant(s) enrollment may proceed but total trial size is expected not to exceed 24 participants.

2.5 Data Source

All data for this study utilized for analyses as outlined in this SAP are collected using the National Eye Institute's (NEI) Electronic Medical Record system (EMR), except graded optical coherency tomography and microperimetry data which are not expected to be graded prior to the analyses as outlined in the SAP. The NEI EMR data files are transferred and uploaded daily into the Coordinating Center's database, with the exception of laboratory data, which is uploaded as requested and, if data are still pending, after closeout of a site and at the completion of all study visits.

3 GENERAL STATISTICAL CONSIDERATIONS

3.1 General Analysis Specifications

3.1.1 Global Analysis Principles

All continuous variables will be summarized using the following descriptive statistics: number of non-missing observations, mean, standard deviation (SD), median, minimum, and maximum. For categorical parameters, descriptive statistics will include the frequency and percentage of participants and eyes for parameters summarized at the participant- and eye-level, respectively. Denominators for percentages will be the number of participants and eyes for parameters summarized at the participant- and eye-level, respectively, in each cohort and overall in the respective population with data at the respective visit, unless otherwise specified.

The baseline value will be the average of the Baseline 1 and Baseline 2 visit values when calculating change from baseline. Change from baseline will be calculated as the value at the follow-up visit minus the baseline value. As of Amendment V (IRB approved February 27, 2020), a Baseline 3 visit was added to provide confirmation of recovery from the Ozurdex injection prior to administration of IP and to evaluate for any change to the baseline parameters listed above following Ozurdex administration. At the time of finalization of v1.0 of the SAP, no participants were enrolled subsequent to the approval of this amendment and therefore Baseline 3 visits were not completed for any enrolled participants.

Manifest refraction values will be utilized, if available, for assessments of visual acuity. If manifest refraction values are not available, visual acuity measurements obtained from last manifest refraction will be utilized.

3.1.2 Reporting Conventions

In general, all data listed will be sorted by cohort, participant and, when appropriate, time point within participant. Summary tables will present results by cohort and eye, and overall (across cohorts and/or eyes), where appropriate. The associated dose (in vector genomes) for each cohort is provided in **Table 2**.

The mean, SD, and median will be reported to one decimal place regardless of the number of decimals used for the original data. The minimum and maximum will be reported to one decimal point unless the data are reported in whole numbers, in which case the minimum and maximum will be reported in whole numbers.

Percentages will be reported to the nearest whole number; values greater than zero and <1% will be presented as "<1"; values less than 100% and greater than 99% will be reported as ">99". Zero counts will be displayed as "0" and corresponding percentages will not be reported to avoid redundancy, unless otherwise specified.

"NA" will be used to denote cells that are not applicable, including for reporting SDs where the number of observations is one and for displaying values that are structurally zero (i.e., values that will always be zero). "NE" (meaning Not Estimable) will be used for any summaries or statistics that could not be estimated or are undefined (e.g., due to dividing by zero). Missing values will be presented as blank in listings. In tables, when the sample size is zero, the sample size (N) will be presented as "0" and all other summary statistics will be blank.

For all other estimators, results will be presented with no more precision than is of scientific value and is meaningful.

3.1.3 Analysis Software and Other Technical Details

Statistical analyses will be performed, and all tables, figures, and listings presented in the analyses will be created using SAS v9.4 or higher or R v4.3.2 or higher.

3.2 Analysis Populations

The following analysis populations will be considered:

Enrolled population: Includes all participants enrolled in the study, regardless of follow up or receipt of the AAV vector injection. This population will be utilized for presentations corresponding to participant history and study conduct.

Safety population: Includes all participants enrolled in the study and were administered the AAV vector injection, regardless of follow-up. This population will be utilized for presentations corresponding to safety outcome analysis and analyses of ophthalmic examinations.

Of note is that all enrolled participants received the AAV vector injection and therefore the enrolled and safety population are the same.

3.3 Reporting Periods for Adverse Events

Adverse events will be categorized by reporting period as follows:

Immediate Safety Follow-Up: Day 0 (injection day, within 24 hours) through Day 7, inclusive of both these dates

Early Post-Surgery Safety Follow-Up: Day 8 through Year 2, inclusive

Long-Term Safety Follow-Up: after Year 2 through end of study participation

3.4 Subgroups, Interactions, and Covariates

The protocol does not define any formal subgroup analyses, and the study is not powered to perform subgroup analyses.

3.5 Handling of Missing Data

In general, any missing data will be assumed to be missing completely at random and will not be imputed.

3.6 Multiple Comparisons/Multiplicity

Analyses will be descriptive in nature. No adjustments for multiplicity are planned, but the number of comparisons made for the primary analysis will be factored into the interpretation of results, as appropriate.

3.7 Handling of Duplicate Assessments

If participants completed assessments at both scheduled and supplementary visits, the assessments from the scheduled visit will be considered in the tabular summaries and figures. However, if an assessment is completed only at supplementary visits, then the assessments from the earliest supplementary visit will be included in the tabular summaries and figures. Results of all assessments, including those performed during supplementary visits, will be included in listings.

4 SUMMARY OF STUDY CONDUCT AND PARTICIPANTS

All presentations in this section will be based on the enrolled population.

4.1 Disposition of Participants

Overall participant disposition, including the number and percentage of participants enrolled; administered the AAV vector injection; completed follow-up through Month 18, Year 5, and Year 15; and discontinued the study early or per-protocol will be summarized by cohort and overall (**Table 3**).

A listing of participants early terminations, along with the reason for termination, and study completions will be presented as well as the number of years from injection date of the early termination/study completion **(Listing 1).** If a second site is activated, a CONSORT diagram showing participant flow will also be presented (**Figure 1**).

4.2 Demographic and Other Baseline Characteristics

Demographics characteristics, including age at baseline, sex, ethnicity, and race will be summarized by cohort and overall (**Table 4**) and listed (**Listing 2**). The listing will also include other baseline characteristics including the registration date, the eye selected to be the study eye, and the dose cohort for each participant.

4.3 Medical and Ocular History

If a second site is activated, a history of select medical conditions, ocular conditions, and ocular procedures will be listed for each participant. The listing will include relevant dates, where applicable (**Listing 3**).

4.4 Prior and Concomitant Medications

Prior and concomitant medications will be coded to the Anatomical Therapeutic Classification using the World Health Organization (WHO) Drug Dictionary. If a second site is activated, a summary by first and second Anatomical Therapeutical Chemical (ACT) level code (i.e., ATC1 and ACT2, respectively) by cohort and overall (**Table 5**) and a listing of participant usage of prior and concomitant medications will be presented (**Listing 4**).

4.5 Investigational Product (IP) Administration

Information relating to AAV vector injections will be listed by participant (**Listing 5**). This listing will include the cohort and corresponding dose group, the date of injection, the eye that was injected (treated), any injection complications, and the level of pain at discharge.

4.6 Protocol Deviations, Unanticipated Problems and Non-Compliance

Effective July 1, 2019, with the implementation of the National Institutes of Health (NIH) Intramural Research Program Policy 801, protocol deviations and unanticipated problems are classified by the Investigator as major or minor at the time of data entry (as opposed to serious or not serious), and seriousness of major deviations and unanticipated problems is determined after review by the NIH Institutional Review Board (IRB).

If a second site is activated, the total number of participant-specific protocol deviations, unanticipated problems, and non-compliance events and the number and percentage of participants with deviations, unanticipated problems, and non-compliance events will be summarized by cohort and overall (**Table 6**). If a second site is activated and sufficient data are available, the total number of non-participant specific protocol deviations, unanticipated problems, and non-compliance events will be summarized by cohort and overall (**Table 7**)**.** The type (minor, serious, or not serious) and outcome of events will also be summarized in the aforementioned tables. Listings of participant-specific and non-participant-specific protocol deviations, unanticipated problems and non-compliance events will be presented (**Listings 6-11**).

4.7 Study Procedure Deviations

If a second site is activated and a sufficient number of procedures are missed, a table summarizing the expected number of procedures and the number and percentage of missed procedures, and percentage of procedures missed a) cumulatively for all participants by procedure and b) cumulatively for all participants considering all procedures will be presented (**Table 8**).

A missed procedure is defined when the site reports a missed procedure or when the protocol monitors note a missed procedure at a site visit. The expected number of procedures is defined based on the study flowsheet included in the protocol. The percentage of procedures missed will be calculated as follows:

$$(N_{\text{missed procedures}} / N_{\text{expected procedures}}) * 100.$$

4.8 Visit Schedule Deviations

If a second site is activated, a table summarizing the number of expected follow-up visits (i.e., the number of visits in the study flowsheet expected for each participant based on the timing of their termination) and the number and percentage of missed and out of window follow-up study visits cumulatively and by participant will be presented (**Table 9**). Summary statistics for each cohort and overall will also be presented.

The number of expected follow-up visits and the respective visit window will be calculated from the schedule of activities in the protocol. Expected follow-up visits will either be completed or missed; completed visits will either be inside or out of the visit window. The percentage of missed follow-up study visits will be calculated as:

$$(N_{\text{missed visits}} / N_{\text{expected visits}}) * 100$$

Similarily, the percentage of out of window follow-up study visits will be calculated as:

$$(N_{\text{out of window visits}} / N_{\text{expected visits}}) * 100$$

Baseline visits will not be included in the above calculations as these are pre-requisites for successful enrollment.

4.9 Suspension Rule Assessment

Suspension rule criteria (listed in **Section 2.1.1.**) is assessed throughout the study period. The suspension rule assessment will be summarized by cohort and overall (**Table 10**) and will be listed for each participant (**Listing 12**).

5 SAFETY EVALUATION

These presentations will be based on the safety population. All relevant information will be listed. Outcome measurements or relevant change in outcome measurements will be plotted against time if specified in subsequent subsections.

5.1 Adverse Events (AEs)

Total number and percentage of participants with AEs and number of AEs will be summarized by reporting period (defined in **Section 3.3**), severity, ocular specification, and relatedness to IP (**Table 11**). AEs will also be summarized by Medical Dictionary for Regulatory Activities (MedDRA) system organ class (SOC) and preferred term (PT) (**Table 12**).

All partcipants who experienced any AE will be listed (**Listing 13**). In addition, participants who experienced serious adverse events (SAEs) will be listed separately (**Listing 14**). A listing of participants who experience natual progressions of the disease will also be reported (**Listing 15**).

Individual participant profile plots for participants reporting AEs will be presented indicating the AEs experienced and details of the AE including the PT, study day on which the AE started, duration, severity, relatedness to IP, and whether the AE was an SAE (**Figure 2**).

5.2 Analysis of Primary Safety Endpoint

The primary objective is the safety and tolerability of the AAV8-scRS/IRBP-hRS vector. The analysis of the primary outcome will be descriptive by cohort and overall; no formal hypothesis testing will be performed. These presentations will be based on the safety population.

The following outcomes will be summarized for the corresponding reporting periods defined above (**Section 3.3**):

1. Adverse events affecting ocular function that differ clinically from those expected in the normal course of progression of XLRS including:
    a. ≥ 10 EVA letters in best-corrected visual acuity (BCVA) (> 0.2 logMAR) from average of Baseline 1 and Baseline 2 BCVA (Immediate Safety Follow-Up and Early Post-Surgery Safety Follow-Up reporting periods together).
    b. Decrease in ERG response amplitude by ≥ 75% from average of amplitudes from Baseline 1 and 2 (Immediate Safety Follow-Up and Early Post-Surgery Safety Follow-Up reporting periods together).
    c. Severe ocular inflammation beyond that inflammation anticipated consequent to an intravitreal injection (Early Post-Surgery Safety Follow-Up reporting period).*

d. Adverse events deemed clinically-related to the intraocular administration technique will also be noted and reported, including vitreous hemorrhage, retinal detachment, intraocular pressure elevation, lens damage and endophthalmitis (Early Post-Surgery Safety Follow-Up reporting period).*

e. Abnormal findings of serum chemistry, hematology, liver function tests or urinalysis/urine chemistry that are beyond Grade 1 (CTCAE v5.0) and/or clinically significantly different than baseline regardless of potential relationship to the AAV vector (Immediate Safety Follow-Up and Early Post-Surgery Safety Follow-Up reporting periods together).

*Details of AEs that may contribute to the respective outcome will be provided to the sponsor who will determine, for each AE, whether it contributes to the respective outcome.

Outcomes a-d will be contribute to the primary endpoint only if they occur in the study eye. Specifically, for each outcome, the following summaries will be provided: the number of events, the number of participants with events, the percentage and associated exact 95% Clopper-Pearson confidence intervals (CIs) of participants with events (**Table 13**). A listing of all the participants who experience any of the outcomes above will be presented and details of the events included as appropriate (**Listing 16**).

5.3 Analysis of Secondary Safety Endpoints

The following secondary outcomes of visual function will be presented for each participant and tabulated over time for both the study eye and fellow eye for all three reporting periods together (see **Section 3.3**). Outcome measurements or relevant change in outcome measurements will be plotted by cohort and eye over time as outlined in subsequent subsections. For these analyses, the safety population will be used. Change from baseline will be calculated as described in **Section 3.1.1**.

5.3.1 Electroretinography

ERG and change in ERG combined response amplitudes from an average of the two baseline measurements and/or change in the b/a-wave amplitude ratio will be listed. Descriptive statistics of change from the average of the two baseline measurements for each ERG amplitude will be summarized by cohort, visit, and eye and if a second site is activated, mean change from baseline plots (± 1 standard deviation [SD]) by cohort and eye will be presented for each ERG amplitude. The following amplitudes and implicit time for the ERG will be separately presented:

- DA Rod (**Listing 17, Table 14, Figure 3-4**)
- DA Comb 0dB (**Listing 18**)
    - DA Comb A 0dB (**Table 15, Figure 5-6**)
    - DA Comb B 0dB (**Table 16, Figure 7-8**)
- DA Comb 11dB (**Listing 19**)
    - DA Comb A 11dB (**Table 17, Figure 9-10**)
    - DA Comb B 11dB (**Table 18**, **Figure 11-12**)
- DA O.P.s (**Listing 20, Table 19, Figure 13-14**)
- LA Cone (**Listing 21**)
    - LA Cone B 0dB (**Table 20, Figure 15-16**)

- LA Cone A 11dB (**Table 21, Figure 17-18**)

- LA Flicker (**Listing 22, Table 22, Figure 19-20**)

In listings, "0" indicates a non-recordable response.

5.3.2 Visual Acuity

Visual acuity measurements will be performed using EVA and ETDRS as described in the protocol with EVA being the primary method of data collection. Descriptive statistics of change in BCVA total letters read (as measured by EVA) compared to the average of the two baseline measurements will be summarized by cohort, visit, and eye (**Table 23**). If a second site is activated, box plots of the change from baseline by cohort and eye (**Figure 21-22**) and mean change from baseline (± 1 SD, **Figure 23**) will also be presented graphically**.** A listing of the BCVA total letters read as measured by EVA and change from baseline for all participants (**Listing 23**) and, if a second site is activated, participant and eye-specific spaghetti plots for all participants with separate panels for each cohort (**Figure 24-25**) will be presented. A listing of the BCVA total letters read as measured by ETDRS and change from baseline for all participants will also be presented (**Listing 24**).

5.3.3 Optical Coherence Tomography (OCT)

As mentioned in **Section 2.5**, OCT data are not expected to be graded prior to the analyses as outlined in the SAP. Therefore, completion of OCT imaging will be summarized by eye and cohort at each visit for which it was required per-protocol and overall (**Table 24**) and listed (**Listing 25**).

5.3.4 Microperimetry (MP-1)

As mentioned in **Section 2.5**, MP-1 data are not expected to be graded prior to the analyses as outlined in the SAP. Completion of MP-1 imaging will be summarized by eye and cohort at each visit for which it was required per-protocol and overall (**Table 25**) and listed (**Listing 26**).

5.4 Other Safety Evaluations

These presentations will be based on the safety population, unless otherwise specified, and will include data from all three reporting periods together (see **Section 3.3**). All relevant information will be listed. Outcome measurements or relevant change in outcome measurements will be plotted against time as outlined in subsequent subsections.

5.4.1 Immunosuppressive Regimen

5.4.1.1 Oral Immunosuppressive Regimen

Prior to Amendment Q, approved February 1, 2019, participants could be put on an oral immunosupressive regimen to help with the post-injection inflammation, which they would gradually taper off. Prior to Amendment J, approved December 14, 2016, this regimen consisted of only prednisone. With Amedment J, cyclosporine and mycophenolate mofetil were added to the regimen.

Information related to the oral immunosuppressive regimen consisting of doses of prednisone, cyclosporine, and mycophenolate taken throughout the study will be summarized (**Table 26**). This table will include the medication name, medication start date, medication stop date, maximum daily dose, duration of time on medication, and mean daily dose for each participant. Additionally, doses of each immunosuppressive medication will be listed over time for participants who took them (**Listing 27**).

5.4.1.2 Ozurdex or Triesence Injection

With Amendment Q, approved February 1, 2019, the approach to immune suppression was modified to include the use of prophylactic Ozurdex instead of a multi-agent oral immunosuppressive regimen.

Three to 14 days before the planned day of injection, participants received an injection of Ozurdex (dexamethasone 0.7 mg) in the study eye. Triesence (triamcinolone acetonide, 2-4 mg) will be substituted for Ozurdex given the possibility, in such cases, of migration of the Ozurdex implant into the anterior chamber where it can cause corneal edema.

All participants who received an Ozurdex injections will be listed (**Listing 28**). This listing will include the date and visit the injection was administered along with which medication was used and whether there were any complications.

5.4.2 Anterior Chamber (AC) Tap

An anterior chamber (AC) tap was added to the protocol in Amendment Q, approved February 1, 2019. AC taps are scheduled at the Baseline 2, Day 14, Month 1, and Month 3 visits, but were also able to be performed anytime between Day 14 and Month 18. Based on the amendment approval date, only participants were eligible to receive AC taps per-protocol will be presented (**Listing 29**).

5.4.3 Intraocular Pressure

IOP is assessed at baseline and all follow-up visits to Year 5 in both eyes. IOP measurements at each visit (**Listing 30**) and change from the average of the baseline visits at each follow-up visit will be summarized by cohort, visit and eye (**Table 27**). Mean change in IOP from the average of the two baseline visits will also be presented over time by cohort and eye (**Figure 26**). Spaghetti plots for all participants will also be presented by cohort (**Figure 27-28**).

5.4.4 Laboratory Assessments

Laboratory assessments will be listed for each participant at each visit, indicating if there were any abnormal labs, details of any abnormal labs, any change from baseline and if the change is clinically significant (**Listing 31**). A summary of abnormal laboratory assessments by cohort, visit, and category for participants in the safety population at select visits will be presented (**Table 28**). A listing of the laboratory values that were not considered within the normal range for participants in the safety population with the corresponding CTCAE (v5.0) event and grade as appropriate will be reported (**Listing 32**). Participants are not required to fast prior to visits; therefore, high glucose values reported will be non-fasting glucose levels.

5.4.5 Additional Ophthalmic Assessments

Results of additional ophthalmic assessments such as anterior chamber cells, anterior chamber flare, vitreous cells, vitreous haze, Weiss ring, vitreous separation, and optic nerve edema will be presented as a listing by participant (**Listing 33**).

5.4.6 Telephone Follow-up Assessments

Telephone follow-up assessments are to be performed annually starting at Year 6. At these assessments, participants were asked to report any AEs experienced in the previous year, specifically those related to malignancy, hematological events, neurological events, and autoimmune events, as well as new procedures and any significant ocular changes. The results from the telephone follow-up assessments will be presented as a listing by participant as applicable (**Listing 34**).

6 INTERIM ANALYSES AND DATA MONITORING

No formal interim analysis will take place which requires group sequential methods or adjustment of p-values to control Type I error for this Phase I/IIa clinical trial. However, the NEI DSMC reviewed data accumulated through the Month 1 visit from all participants enrolled after Participant 009 before additional participants were enrolled. Following review of data, the NEI DSMC recommended enrolling additional participants in the current dose cohort (Cohort 4) and for the dose not to exceed 6e11 vg/eye for Cohort 5.

7 SUMMARY OF CHANGES TO THE CONDUCT OF THE STUDY OR PLANNED ANALYSES

Depending on the nature of the data, certain outcomes may be presented differently than outlined in this analysis plan. Tables and figures will be presented only when adequate data are available. Data for graded OCT and microperimetry will not be available to the Coordinating Center at the time of analyses as outlined in the SAP and therefore will not be presented in the report generated based on this SAP.

8 QUALITY ASSURANCE PLANS

To ensure accurate, reliable study results, two statisticians will separately analyze and compare the primary study outcome. All code used to generate primary and secondary outcomes will undergo a code audit by an independent project statistician. All protocol tables, figures, listings, and reports will also undergo review by a secondary statistician or SAS programmer. Documentation of these audits will be kept on file at the Coordinating Center.

APPENDICES

APPENDIX 1. TABLES

LIST OF TABLES

Table 1. Study Flowsheet

VISIT SCHEDULE*	Baseline 1	Baseline 2[1]	Baseline 3	Injection (Day 0)[1]	Day 1	Day 7	Day 14	Month 1	Month 2	Month 3	Month 4	Month 6	Month 9	Month 12	Month 18	Year 2-5[3]
VISIT NUMBER	BL1	BL2	BL3	D00	D01	D07	D14	M01	M02	M03	M04	M06	M09	M12	M18	Y02-Y05
TARGET DAY FROM SURGERY	N/A	N/A	-2 to D00	N/A	1	7	14	30	60	90	120	180	272	365	545	730-1825
VISIT WINDOWS						± 3 days	± 3 days	± 10 days	± 10 days	± 10 days	± 10 days	± 10 days	± 10 days	± 10 days	± 2 months	± 2 months
GENERAL ASSESSMENTS																
Medical / Ophthalmic History	X															
Physical Examination	X[4]	X[4]														
Concomitant Medication and Procedures Assessment	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse Event Assessment			X	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital signs (BP, resp, temp)	X	X	X	X	X	X	X	X	X	X	X					
Telephone Follow-Up																
VISUAL SYSTEM EXAMS (both eyes unless otherwise noted)																
Manifest Refraction [2]	X	X										X		X	X	X
BCVA (EVA and ETDRS)	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X
Microperimetry	X	X						X		X		X	X	X	X	X

Table 1. Study Flowsheet (continued)

VISIT SCHEDULE*	Baseline 1	Baseline 2[1]	Baseline 3	Injection (Day 0)[1]	Day 1	Day 7	Day 14	Month 1	Month 2	Month 3	Month 4	Month 6	Month 9	Month 12	Month 18	Year 2-5[3]
Electroretinography (ERG)	X	X						X		X		X		X	X	X
Optical Coherence Tomography (OCT)	X	X	X				X	X	X	X	X	X	X	X	X	X
Intraocular Pressure (IOP)	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X
Slit Lamp Examination	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X
Fundus Examination	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X
Digital Color Fundus Photography	X											X		X		X
Fluorescein Angiogram (FA)	X[5]	X[5]						X	X		X					
Axial Length Measurement	X															
STUDY INTERVENTION																
Ocular Gene Transfer				X												
LABORATORY																
Complete Blood Count with Differential	X[4]	X[4]		X[8]		X		X	X	X	X	X	X	X	X	
Acute Care, Mineral, and Hepatic Panels	X[4]	X[4]		X[8]		X	X	X	X	X	X	X	X	X	X	
Antibodies to AAV Vector[9]	X[6]	X[6]				X	X	X	X	X	X	X	X	X	X	X[7]
Blood for Storage (including anti-RS1 antibody)[9]	X[6]	X[6]				X	X	X	X	X	X	X	X	X	X	X[7]
Urinalysis	X[4]	X[4]				X		X	X	X	X	X	X	X	X	

Table 1. Study Flowsheet (continued)

VISIT SCHEDULE*	Baseline 1	Baseline 2[1]	Baseline 3	Injection (Day 0) [1]	Day 1	Day 7	Day 14	Month 1	Month 2	Month 3	Month 4	Month 6	Month 9	Month 12	Month 18		Year 2-5[3]
Syphilis testing (RPR and antibody)	X[4]	X[4]															
Tuberculosis testing (PPD or Quantiferon)	X[4]	X[4]															
Hemoglobin A1C	X[4]																
HIV, HBV, and HCV testing	X[4]	X[4]															
Anterior Chamber Tap[10]		X[11]					X	X		X							
Ozurdex Injection		X[12]															

* One or more unscheduled visits for safety assessment can be added based on the discretion of the investigators. In the event that testing is not completed within a day, subsequent clinic visits may be scheduled within the visit window to complete the scheduled evaluation.

** Baseline 3 (BL3) assessments may occur up to two days prior to vector injection or on the same day of and prior to injection.

[1] Baseline 1 (BL1) must occur within 90 days of the injection and Baseline 2 (BL2) must occur within 60 days of the injection.

[2] BCVA with manifest refraction must be performed when scheduled and when there is a change in visual acuity of □ 10 ETDRS letters (□ 0.20 logMAR) from relevant baseline.

[3] Long term follow-up is not part of the primary end point.

[4] These procedures can be performed at either baseline visit, or any day prior to injection. They can also be performed under another NEI study within the 60 days prior to injection.

[5] The baseline FA can be performed at either baseline visit, or under another site study within 9 months prior to injection, provided it includes late phase frames of the optic nerve of each eye.

[6] These procedures can be performed at either baseline visit or any day prior to injection.

[7] Blood for storage and antibodies to AAV vector testing may be drawn at Visits Y02-Y05.

[8] Day 0 laboratory assessments may be performed up to seven days prior to the D00 visit.

[9] Research blood may also be collected as needed.

[10] Anterior chamber tap may also be performed anytime at Investigator discretion up to an additional 3 times between Week 2 and Month 18.

[11] May be performed within two weeks of Baseline 2.Ozurdex injection will be given 3 - 14 days prior to planned vector administration (D00).

Table 2. AAVY-scRS/IRBPhRS Clinical Dose Escalation Scheme

Cohort*	Dose in Vector Genomes (vg)†
1	1e9
2	1e10
3	1e11
4	1e11
5	3e11
6	Not to exceed 6e11

* Up to six participants may be enrolled into each dose cohort based on DMC review and recommendation as described in Section 6 of the protocol.
† All injection volumes will be 0.05 mL to achieve the proper dose based on dilution in the pharmacy.

Table 3. Disposition (Enrolled Population)

Disposition	Cohort 1 (N=X) N (%)	Cohort 2 (N=X) N (%)	Cohort 3 (N=X) N (%)	Cohort 4 (N=X) N (%)	Cohort 5 (N=X) N (%)	Total (N=X) N (%)
Enrolled	x	x	x	x	x	x
Administered AAV Vector Injection	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Enrollment Through Month 18						
Terminated study prior to Month 18	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
AE/intercurrent illness	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Death	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Insufficient Therapeutic Response	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Lost to follow-up	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Participant request/refusal	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Early study closure	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Protocol deviation	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Other	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Completed Month 18 Visit	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Month 18 Through Year 5[a]						
Terminated study at or after Month 18 and prior to Year 5[a]	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
AE/intercurrent illness	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Table 3. Disposition (Enrolled Population) (continued)

Disposition	Cohort 1 (N=X) N (%)	Cohort 2 (N=X) N (%)	Cohort 3 (N=X) N (%)	Cohort 4 (N=X) N (%)	Cohort 5 (N=X) N (%)	Total (N=X) N (%)
Death	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Insufficient Therapeutic Response	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Lost to follow-up	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Participant request/refusal	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Early study closure	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Protocol deviation	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Other	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Completed Year 5[a] Visit	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Year 5[a] Through Year 15						
Completed study at or after Year 5[a] and prior to Year 15	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Terminated study at or after Year 5[a] and prior to Year 15	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
AE/intercurrent illness	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Death	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Insufficient Therapeutic Response	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Lost to follow-up	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Participant request/refusal	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Table 3. Disposition (Enrolled Population) (continued)

Disposition	Cohort 1 (N=X) N (%)	Cohort 2 (N=X) N (%)	Cohort 3 (N=X) N (%)	Cohort 4 (N=X) N (%)	Cohort 5 (N=X) N (%)	Total (N=X) N (%)
Early study closure	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Protocol deviation	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Other	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Completed Year 15 Visit	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
Column header counts and denominators are the number of participants in the enrolled population in each cohort and overall. Percentages are rounded to the nearest whole number.
[a] Minimum required follow-up is through Year 5. Prior to Amendment X (Institutional Review Board approved on March 24, 2022), additional follow-up beyond Year 5 may be completed for those participants enrolled at the beginning of the study. As of Amendment X, participants could complete the study per-protocol at Year 5.

Table 4. Participant Demographics Characteristics (Enrolled Population)

	Cohort 1 (N=X)	Cohort 2 (N=X)	Cohort 3 (N= X)	Cohort 4 (N= X)	Cohort 5 (N= X)	Total (N= X)
Age Category (years) at Baseline, N (%)						
18-29	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
30-39	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
40-49	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
50-59	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
60-69	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
70-79	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
>79	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Age (years) at Baseline						
N	x	x	x	x	x	x
Mean (SD)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Range (Min, Max)	(xx, xx)	(xx, xx)	(xx, xx)	(xx, xx)	(xx, xx)	(xx, xx)
Sex, N (%)						
Male	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Ethnicity, N (%)						
Hispanic or Latino	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Not Hispanic or Latino	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Table 4. Participant Demographics Characteristics (Enrolled Population) (continued)

	Cohort 1 (N=X)	Cohort 2 (N=X)	Cohort 3 (N= X)	Cohort 4 (N= X)	Cohort 5 (N= X)	Total (N= X)
Unknown	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Race, N (%)						
American Indian or Alaskan Native	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Asian	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Black	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Hawaiian or Pacific Islander	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
White	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Multiple Race	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Unknown	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
Column header counts and denominators are total number of participants in the enrolled population in each cohort and overall. Percentages are rounded to the nearest whole number.

Table 5. Prior and Concomitant Medications (Enrolled Population)

WHO Drug Code Level 1, Anatomic Group[a]	WHO Drug Code Level 2, Therapeutic Group	Cohort 1 (N=X) N (%)	Cohort 2 (N=X) N (%)	Cohort 3 (N=X) N (%)	Cohort 4 (N=X) N (%)	Cohort 5 (N=X) N (%)	Total (N=X) N (%)
Any Level 1 Codes	Any Level 2 Codes	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
[ATC Level 1 – 1]	Any [ATC 1 – 1]	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	[ATC 2 – 1]	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	[ATC 2 – 2]	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	[ATC 2 – 3]	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
[ATC Level 1 – 2]	Any [ATC 1 – 2]	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	[ATC 2 – 1]	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	[ATC 2 – 2]	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	[ATC 2 – 3]	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
Column header counts and denominators are total number of participants in the enrolled population in each cohort and overall. Percentages are rounded to the nearest whole number.
[a] WHO Drug Dictionary Version September 2022

Table 6. Participant Specific Protocol Deviations, Unanticipated Problems, and Non-Compliance (Enrolled Population)

	Cohort 1 (N=X)		Cohort 2 (N=X)		Cohort 3 (N=X)		Cohort 4 (N=X)		Cohort 5 (N=X)		Total (N=X)	
	Part. with Events N (%)	No. of Events N	Part. with Events N (%)	No. of Events N	Part. with Events N (%)	No. of Events N	Part. with Events N (%)	No. of Events N	Part. with Events N (%)	No. of Events N	Part. with Events N (%)	No. of Events N
All events	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x
Protocol deviations	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x
Unanticipated problems	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x
Non-compliance	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x
Type[a]												
Minor	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x
Not serious	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x
Serious	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x
Outcome												
Participant follow-up continues	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x

Table 6. Participant Specific Protocol Deviations, Unanticipated Problems, and Non-Compliance (Enrolled Population) (continued)

	Cohort 1 (N=X)	Cohort 2 (N=X)	Cohort 3 (N=X)	Cohort 4 (N=X)	Cohort 5 (N=X)	Total (N=X)	Cohort 1 (N=X)	Cohort 2 (N=X)	Cohort 3 (N=X)	Cohort 4 (N=X)	Cohort 5 (N=X)	Total (N=X)
	Part. with Events N (%)	No. of Events N	Part. with Events N (%)	No. of Events N	Part. with Events N (%)	No. of Events N	Part. with Events N (%)	No. of Events N	Part. with Events N (%)	No. of Events N	Part. with Events N (%)	No. of Events N
Participant follow-up terminated	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x
Investigational product remains stable	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x
Investigational product returned or discarded	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x
Other	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
Column header counts and denominators are total number of participants in in the enrolled population in each cohort and overall. Percentages are rounded to the nearest whole number.
[a] Investigators classify deviations and unanticipated problems as minor or major and IRB classifies the major deviations and unanticipated problems as serious or not serious.

Table 7. Non-Participant Specific Protocol Deviations, Unanticipated Problems, and Non-Compliance

This table will be similar to Table 6 but will not include cohort-specific columns and will exclude the “Part. with Events N (%)” columns.

Table 8. Missed Procedures (Enrolled Population)

	Cohort 1 (N=X)		Cohort 2 (N=X)		Cohort 3 (N=X)		Cohort 4 (N=X)		Cohort 5 (N=X)		Total (N=X)	
	Expected N[a]	Missed N (%)[b]	Expected N[a]	Missed N (%)[b]	Expected N[a]	Missed N (%)[b]	Expected N[a]	Missed N (%)[b]	Expected N[a]	Missed N (%)[b]	Expected N[a]	Missed N (%)[b]
By Participant												
Cohort 1												
XXXXXX	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)
XXXXXX	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)
…												
Total	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)
Cohort 2												
XXXXXX	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)
XXXXXX	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)
…												
Total	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)
By Procedure												
Acute Care, Mineral, and Hepatic Panels	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)

Table 8. Missed Procedures (Enrolled Population) (continued)

	Cohort 1 (N=X)		Cohort 2 (N=X)		Cohort 3 (N=X)		Cohort 4 (N=X)		Cohort 5 (N=X)		Total (N=X)	
	Expected N[a]	Missed N (%)[b]	Expected N[a]	Missed N (%)[b]	Expected N[a]	Missed N (%)[b]	Expected N[a]	Missed N (%)[b]	Expected N[a]	Missed N (%)[b]	Expected N[a]	Missed N (%)[b]
Adverse Event Assessment	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)
…												
Total	**xx**	**xx (xx)**	**xx**	**xx (xx)**	**xx**	**xx (xx)**	**xx**	**xx (xx)**	**xx**	**xx (xx)**	**xx**	**xx (xx)**

[a] Number of expected procedures is defined based on the study flowsheet included in the protocol.
[b] Number of missed procedures is defined when the site reports a missed procedure or when the protocol monitors note missed procedures at a site visit. Denominators are the number of expected procedures for each cohort or overall. Percentages are rounded to the nearest whole number.

Table 9. Missed and Out of Window Follow-Up Study Visits (Enrolled Population)

Cohort	Participant ID	Expected N[a]	Missed N (%)[b]	Out of Window N (%)[b]	Visits Missed or Out of Window
1	XXXXXX	x	x (x)	x (x)	xxx, xxx
	XXXXXX	x	x (x)	x (x)	xxx, xxx
	XXXXXX	x	x (x)	x (x)	xxx, xxx
…					
	Total	**x**	**x (x)**	**x (x)**	
2	XXXXXX	x	x (x)	x (x)	xxx, xxx
	XXXXXX	x	x (x)	x (x)	xxx, xxx
	XXXXXX	x	x (x)	x (x)	xxx, xxx
	Total	**x**	**x (x)**	**x (x)**	
…					
All	**Total**	**x**	**x (x)**	**x (x)**	

[a] The expected number of follow-up visits is based on the schedule of activities.
[b] Denominators are the number of expected follow-up visits. Percentages are rounded to the nearest whole number.

Table 10. Summary of Suspension Rule Assessments by Cohort

Cohort	Decrease in Visual Function[a]		Endophthalmitis	Anterior Chamber[d]	Vitreous Reaction[e]	Optic Nerve Edema[f]	Retinitis[g]	Systemic Response[h]	Serious Adverse Event[i]
	Visual Acuity[b]	ERG Amplitude[c]							
1	xx	xx	xx	xx	xx	xx	xx	xx	xx
2	xx	xx	xx	xx	xx	xx	xx	xx	xx
3	xx	xx	xx	xx	xx	xx	xx	xx	xx
4	xx	xx	xx	xx	xx	xx	xx	xx	xx
5	xx	xx	xx	xx	xx	xx	xx	xx	xx
Total	xx	xx	xx	xx	xx	xx	xx	xx	xx

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
Ophthalmic occurrences are assessed for the study eye. Baseline values are the average of the two baseline visits.
Abbreviations: ERG-Electroretinogram
[a] A significant decrease in visual function, unless this decline is attributable to ocular surface effects or due to minimal inflammation (anterior chamber pigmented or nonpigmented cells of grade 1+ or less) from the intravitreal injection procedure during the first 10 days following administration of the investigational product
[b] Decrease in best corrected visual acuity of ≥ 10 Early Treatment Diabetic Retinopathy Study letters
[c] Decrease in ERG response amplitude (DA Rod, DA Comb A 0dB, DA Comb B 0dB, DA Comb A 11dB, DA Comb B 11dB, DA O.P.s, LA Cone B 0dB, LA Cone A 11dB, LA Flicker) ≥ 75%
[d] Anterior chamber cellular reaction of Grade 3+ or higher
[e] Vitreous cellular reaction of Grade 3+ or higher In any portion of the vitreous cavity
f Optic nerve edema of Grade 1+ or higher
[g] Retinitis, retinal vasculitis, or choroiditis
[h] As reflected by Grade 2 lab test or any Grade 3-4 event/laboratory test related to the investigational product
[i] Serious adverse event (SAE) related to the study article

Table 11. Summary of Adverse Events by Cohort

	Cohort 1 (N=X) n (%)	Cohort 2 (N=X) n (%)	Cohort 3 (N=X) n (%)	Cohort 4 (N=X) n (%)	Cohort 5 (N=X) n (%)	Total (N=X) n (%)
Number of Participants with an AE[a]	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Reporting Period						
Immediate Safety Follow-Up	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Early Post-Surgery Safety Follow-Up	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Long-Term Safety Follow-Up	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Severity						
Mild	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Moderate	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Severe	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Eye	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Non-ocular	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Study Eye	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Fellow Eye	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Outcome	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Resolved	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Resolved with sequelae	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Death	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Resolved by convention	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Reasonable Possibility that the Investigational Product Caused the Event	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
No	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
N/A	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
Column header counts are the number of participants in the safety population in the respective cohort or overall. Denominator is the total number of adverse events in the cohort or overall, unless otherwise specified. Percentages are rounded to the nearest whole number and may not add up to 100%.
[a] Denominator is the number of participants in the safety population.

Table 12. Adverse Events by MedDRA System Organ Class and Preferred Term by Cohort

System Organ Class (SOC)[a, b]	Preferred Term (PT)[a]	Cohort 1 (N=X)	Cohort 2 (N=X)	Cohort 3 (N=X)	Cohort 4 (N=X)	Cohort 5 (N=X)	Total (N=X)
xxxx	xxx	xx	xx	xx	xx	xx	xx
	xxx	xx	xx	xx	xx	xx	xx
	Total	**xx**	**xx**	**xx**	**xx**	**xx**	**xx**
xxxx	xxx	xx	xx	xx	xx	xx	xx
	xxx	xx	xx	xx	xx	xx	xx
	Total	**xx**	**xx**	**xx**	**xx**	**xx**	**xx**
Total		**xx**	**xx**	**xx**	**xx**	**xx**	**xx**

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
Abbreviations: PT-Preferred Term; SOC-System Organ Class
Column header counts are the number of participants in the safety population in the respective cohort or overall.
[a] MedDRA Versions XX.
[b] SOCs are presented in descending order of number of events reported overall; PTs within each SOC are also presented in descending order of number of events reported overall.

Table 13. Primary Outcome of Ocular and Systemic Safety Events

	Cohort 1 (N=X)			Cohort 2 (N=X)			Cohort 3 (N=X)			Cohort 4 (N=X)			Cohort 5 (N=X)			Total (N=X)		
Outcome	**n**	**N (%)**	**(95% CI)**	**n**	**N (%)**	**(95% CI)**	**n**	**N (%)**	**(95% CI)**	**n**	**N (%)**	**(95% CI)**	**n**	**N (%)**	**(95% CI)**	**n**	**N (%)**	**(95% CI)**
Adverse event affecting ocular function[a]	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)
Visual acuity[b]	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)
ERG amplitude[c]	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)
Severe ocular inflammation[d]	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)
Clinically related to the intraocular administration technique[e]	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)
Abnormal findings of serum chemistry, hematology, liver function tests or urinalysis/urine chemistry[f]	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)	x	x (x)	(xx, xx)

Abbreviations: CI = confidence interval; BCVA = best corrected visual acuity; ERG = electroretinogram.
Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
Column headers and denominators are total number of participants in the safety population in each cohort and overall. n is the number of events. N is the number of participants with a given event where participants are counted at most once per row and percentages are rounded to the nearest whole number. Exact binomial confidence intervals correspond to the point estimate of the percentage of participants and are calculated using the Clopper-Pearson method.
[a] Includes adverse events that differ clinically from those expected in the normal course of progression of XLRS and belong to one of the sub-outcomes.
[b] Decrease in best corrected visual acuity of ≥ 10 electronic visual acuity letters in the study eye
[c] Decrease in ERG response amplitude (DA Rod, DA Comb A 0dB, DA Comb B 0dB, DA Comb A 11dB, DA Comb B 11dB, DA O.P.s, LA Cone B 0dB, LA Cone A 11dB, LA Flicker) ≥ 75% in the study eye
[d] Beyond inflammation anticipated consequent to an intravitreal injection and occurring in the study eye.
[e] Includes vitreous hemorrhage, retinal detachment, intraocular pressure elevation, lens damage and endophthalmitis occurring in the study eye.
[f] Must be beyond Grade 1 (Common Terminology Criteria for Adverse Events [CTCAE] 4.0) and/or clinically significantly different than baseline regardless of potential relationship to the AAV vector.

Table 14. Summary of Change in DA Rod Over Time by Eye and Cohort

Implementation Note: This will be repeated for each cohort with the dose indicated in the column header (e.g., "Cohort 1 – 1e9").

	Cohort X - XeX (N=X)									
	D01 Δ	**D14 Δ**	**M01 Δ**	**M06 Δ**	**M12 Δ**	**Y02 Δ**	**Y03 Δ**	**Y04 Δ**	**Y05 Δ**	**Y07 Δ**
Study Eye										
Amp (µV)										
N	x	x	x	x	x	x	x	x	x	x
Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Range (Min, Max)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)
Imp (ms)										
N	x	x	x	x	x	x	x	x	x	x
Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Range (Min, Max)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)
Fellow Eye										
Amp (µV)										
N	x	x	x	x	x	x	x	x	x	x
Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Range (Min, Max)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)

Table 14. Summary of Change in DA Rod Over Time by Eye and Cohort (continued)

	Cohort X - XeX (N=X)									
	D01 Δ	**D14 Δ**	**M01 Δ**	**M06 Δ**	**M12 Δ**	**Y02 Δ**	**Y03 Δ**	**Y04 Δ**	**Y05 Δ**	**Y07 Δ**
Imp (ms)										
N	x	x	x	x	x	x	x	x	x	x
Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Range (Min, Max)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)

Abbreviations: Amp-amplitude; Imp-implicit time; ms=millisecond; D01-Day 1; D14-Day 14; M01-Month 1; M06-Month 6; M12-Month 12; Y02-Year 2; Y03-Year 3; Y04- Year 4; Y05-Year 5; Y07-Year 7
Δ indicates change from baseline. Change is computed relative to the average of the two baseline visits.

Table 15. Summary of Change in DA Comb A 0dB Over Time by Eye and Cohort

This table will be similar to Table 14.

Table 16. Summary of Change in DA Comb B 0dB Over Time by Eye and Cohort

This table will be similar to Table 14.

Table 17. Summary of Change in DA Comb A 11dB Over Time by Eye and Cohort

This table will be similar to Table 14.

Table 18. Summary of Change in DA Comb B 11dB Over Time by Eye and Cohort

This table will be similar to Table 14.

Table 19. Summary of Change in DA O.P.s Over Time by Eye and Cohort

This table will be similar to Table 14.

Table 20. Summary of Change in LA Cone B 0dB Over Time by Eye and Cohort

This table will be similar to Table 14.

Table 21. Summary of Change in LA Cone A 11dB Over Time by Eye and Cohort

This table will be similar to Table 14.

Table 22. Summary of Change in LA Flicker Over Time by Eye and Cohort

This table will be similar to Table 14.

Table 23. Summary of Change in Best Corrected Visual Acuity (BCVA) as Measured by Electronic Visual Acuity (EVA) Over Time by Eye and Cohort

This table will be similar to Table 14.

Table 24. Summary of Completion of Optical Coherence Tomography (OCT) Imaging Over Time by Eye and Cohort

	Cohort 1 (N=X)		Cohort 2 (N=X)		Cohort 3 (N=X)		Cohort 4 (N=X)		Cohort 5 (N=X)		Total (N=X)	
Visit	Study Eye N (%)	Fellow Eye N (%)	Study Eye N (%)	Fellow Eye N (%)	Study Eye N (%)	Fellow Eye N (%)	Study Eye N (%)	Fellow Eye N (%)	Study Eye N (%)	Fellow Eye N (%)	Study Eye N (%)	Fellow Eye N (%)
Baseline 1	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)
Baseline 2	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)
Day 14	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)
Month 1	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)	xx	xx (xx)
…												
Total	**xx**	**xx (xx)**	**xx**	**xx (xx)**	**xx**	**xx (xx)**	**xx**	**xx (xx)**	**xx**	**xx (xx)**	**xx**	**xx (xx)**

Denominators are the number of expected OCT assessments for each eye within each cohort or overall. Percentages are rounded to the nearest whole number.

Table 25. Summary of Completion of Microperimetry (MP-1) Imaging Over Time by Eye and Cohort

This table will be similar to Table 24.

Table 26. Immunosuppressive (Prednisone, Cyclosporine, and Mycophenolate) Regimen Summary

Cohort	Participant ID	Injection Date	Medication Name[a]	Medication Start Date	Medication Stop Date[b]	Duration (days)[c]	Maximum Daily Dose (mg)	Mean Daily Dose (mg)	Current Daily Dose (mg)	Reason[d]
x	xxxxxx	xx/xx/xx	xxxxxxx	xx/xx/xx	xx/xx/xx	x	x	xx	x	xxxxxxx
	xxxxxx	xx/xx/xx	xxxxxxx	xx/xx/xx	xx/xx/xx	x	x	xx	x	xxxxxxx
x	xxxxxx	xx/xx/xx	xxxxxxx	xx/xx/xx	xx/xx/xx	x	x	xx	x	xxxxxxx
	xxxxxx	xx/xx/xx	xxxxxxx	xx/xx/xx	xx/xx/xx	x	x	xx	x	xxxxxxx

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
Yellow highlighting corresponds to reasons that are related to ocular inflammation or immunosuppression.
[a] Taken verbatim as entered by site staff.
[b] If the actual medication stop date is missing and the current daily dose is 0, then target date is used as the medication stop date.
[c] Doses may not be continuous, so duration may not be exactly the number of days between the medication start and stop date.
[d] Reason is taken from the medication indication.

Table 27. Summary of Change in Intraocular Pressure (IOP) Over Time by Eye and Cohort

This table will be similar to Table 14.

Table 28. Summary of Frequency of Abnormal Laboratory Assessments by Category, Cohort, and Visit

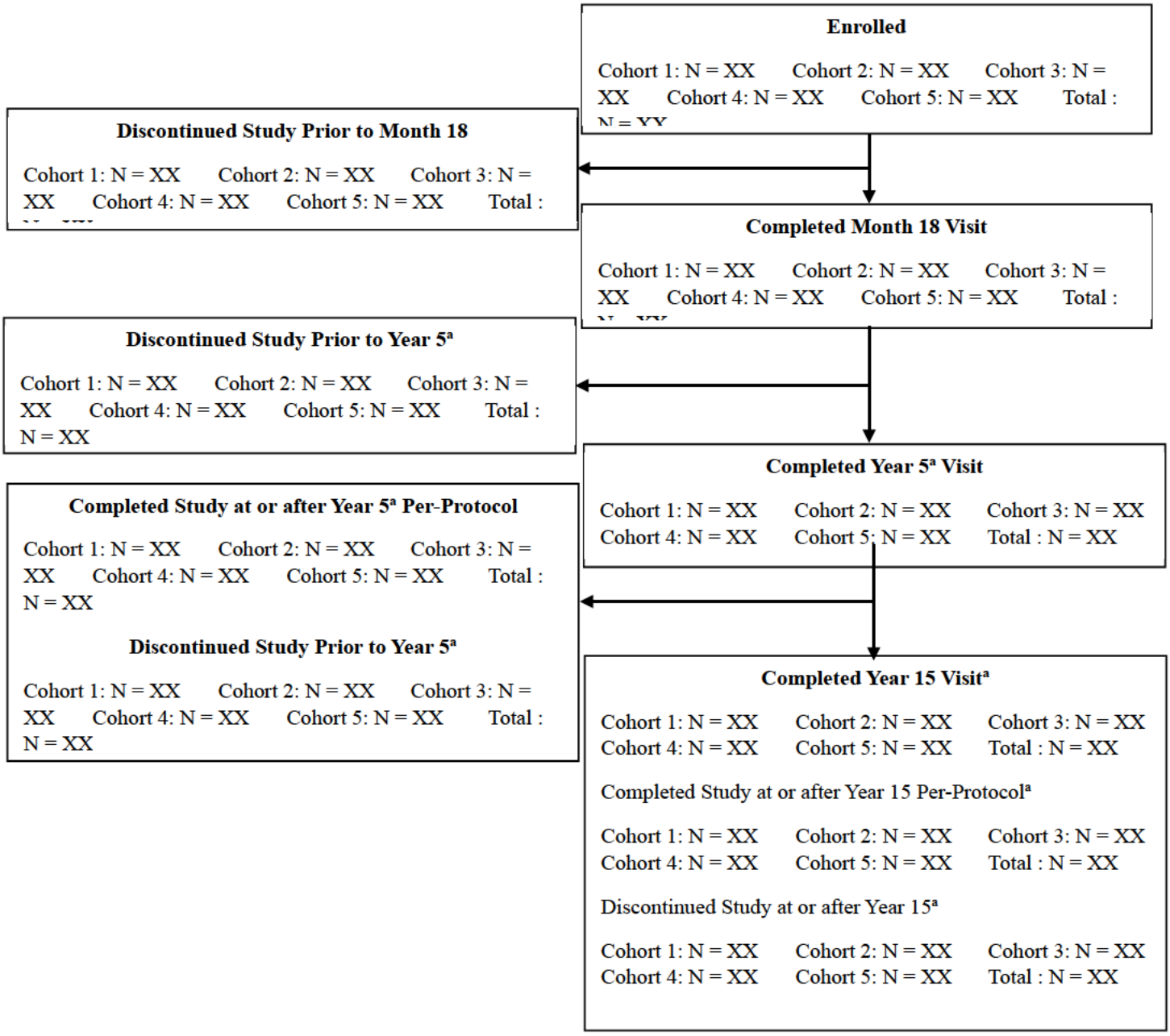
Laboratory Assessment	Visit	Cohort 1 (N=X)	Cohort 2 (N=X)	Cohort 3 (N=X)	Cohort 4 (N=X)	Cohort 5 (N=X)	Total (N=X)
Acute Care Panel	**Baseline 1**	xx	xx	xx	xx	xx	xx
	Baseline 2	xx	xx	xx	xx	xx	xx
	Day 0	xx	xx	xx	xx	xx	xx
	Month 12	xx	xx	xx	xx	xx	xx
	Month 12	xx	xx	xx	xx	xx	xx
Anti-HBc Antibody	**Baseline 1**	xx	xx	xx	xx	xx	xx
	Baseline 2	xx	xx	xx	xx	xx	xx
	…						

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.

APPENDIX 2. FIGURES

LIST OF FIGURES

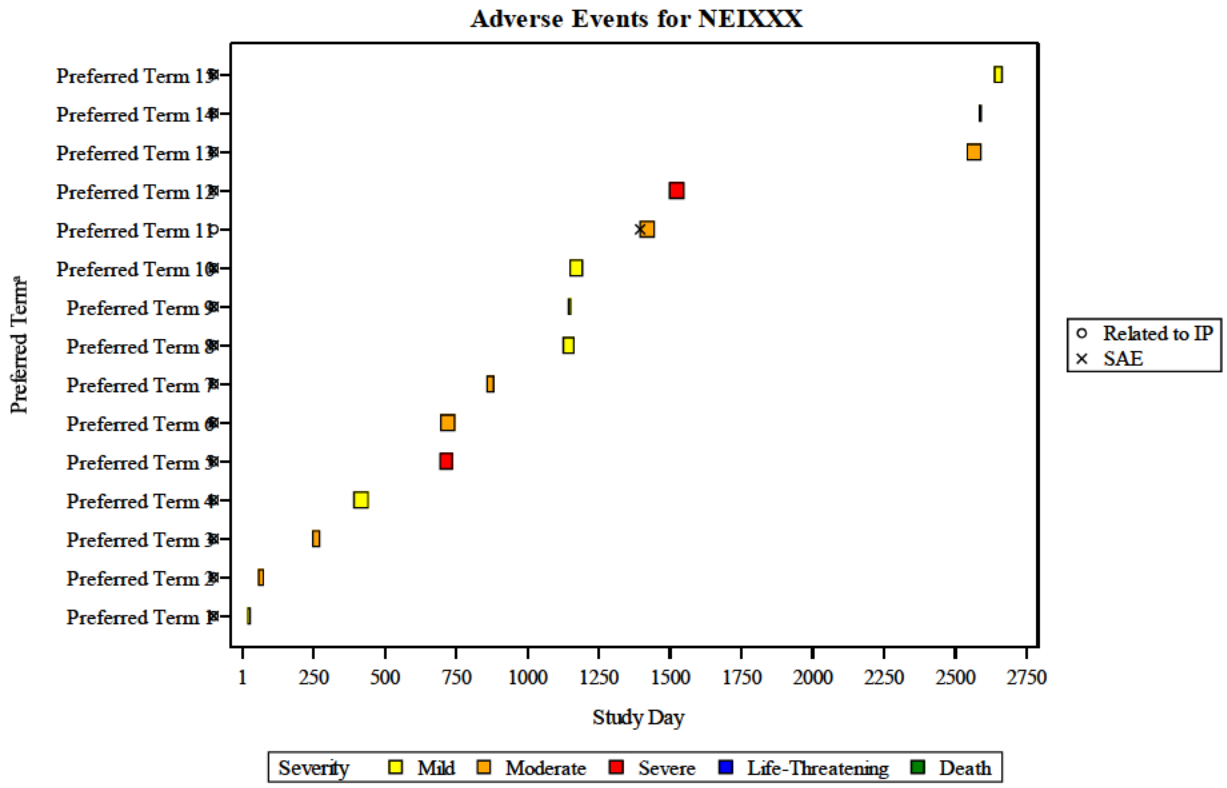
Figure 1. Consort Diagram



[a] Minimum required follow-up is through Year 5. Prior to Amendment X (Institutional Review Board approved on March 24, 2022), additional follow-up beyond Year 5 may be completed for those participants enrolled at the beginning of the study. As of Amendment X, participants could complete the study per-protocol prior at Year 5.

Figure 2. Patient Profiles for Adverse Events

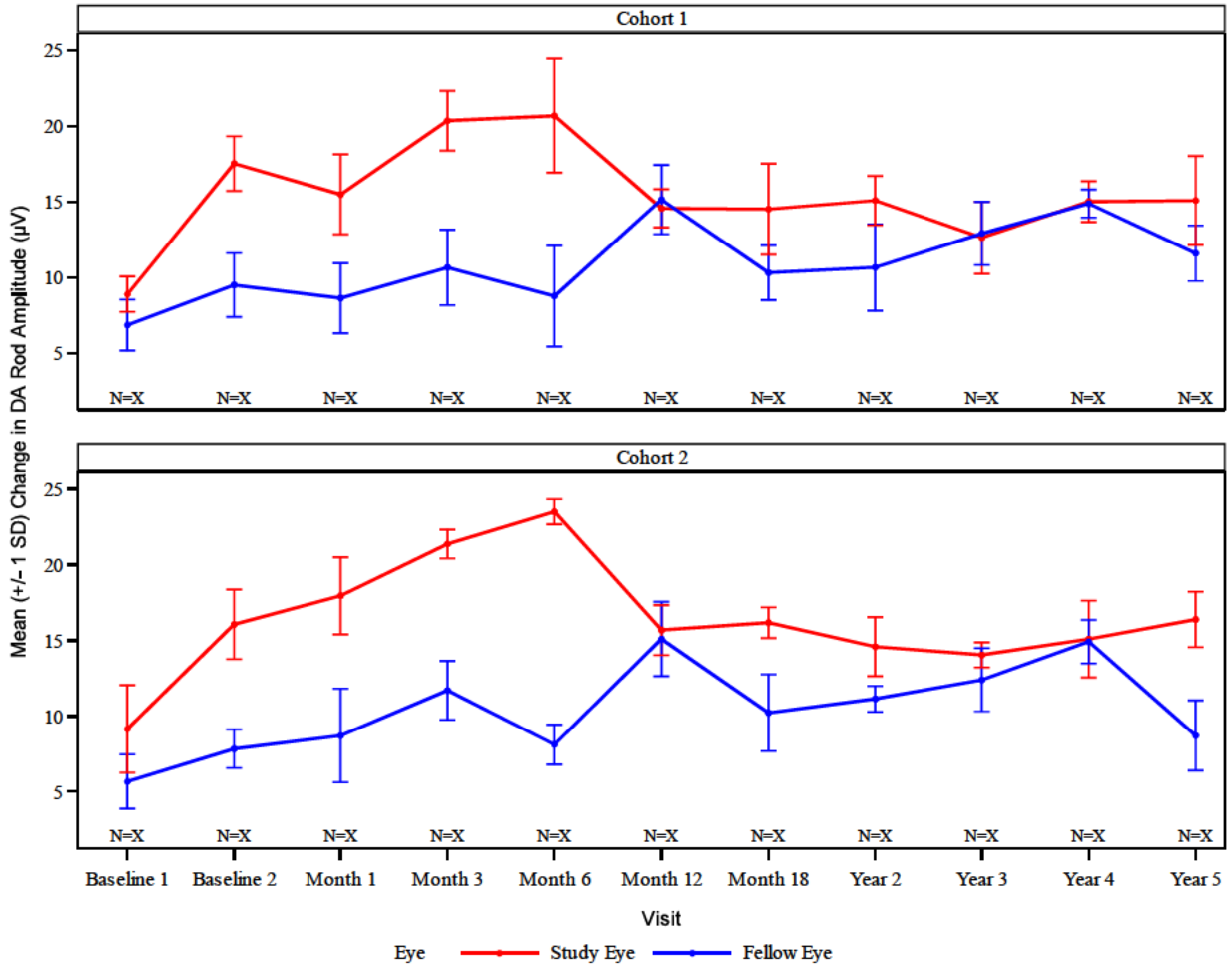
Implementation Note: This is an example figure.



[a] MedDRA Version: XX.X.

Figure 3. Mean Change from Baseline in DA Rod Amplitude by Cohort and Eye

Implementation Note: This is an example figure.



Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye.

Change is computed relative to the average of the two baseline visits.

Figure 4. Mean Change from Baseline in DA Rod Implicit Time by Cohort and Eye

This figure will be similar to Figure 3.

Figure 5. Mean Change from Baseline in DA Comb A 0dB Amplitude by Cohort and Eye

This figure will be similar to Figure 3.

Figure 6. Mean Change from Baseline in DA Comb A 0dB Implicit Time by Cohort and Eye

This figure will be similar to Figure 3.

Figure 7. Mean Change from Baseline in DA Comb B 0dB Amplitude by Cohort and Eye

This figure will be similar to Figure 3.

Figure 8. Mean Change from Baseline in DA Comb B 0dB Implicit Time by Cohort and Eye

This figure will be similar to Figure 3.

Figure 9. Mean Change from Baseline in DA Comb A 11dB Amplitude by Cohort and Eye

This figure will be similar to Figure 3.

Figure 10. Mean Change from Baseline in DA Comb A 11dB Implicit Time by Cohort and Eye

This figure will be similar to Figure 3.

Figure 11. Mean Change from Baseline in DA Comb B 11dB Amplitude by Cohort and Eye

This figure will be similar to Figure 3.

Figure 12. Mean Change from Baseline in DA Comb B 11dB Implicit Time by Cohort and Eye

This figure will be similar to Figure 3.

Figure 13. Mean Change from Baseline in DA O.P.s Amplitude by Cohort and Eye

This figure will be similar to Figure 3.

Figure 14. Mean Change from Baseline in DA O.P.s Implicit Time by Cohort and Eye

This figure will be similar to Figure 3.

Figure 15. Mean Change from Baseline in LA Cone B 0dB Amplitude by Cohort and Eye

This figure will be similar to Figure 3.

Figure 16. Mean Change from Baseline in LA Cone B 0dB Implicit Time by Cohort and Eye

This figure will be similar to Figure 3.

Figure 17. Mean Change from Baseline in LA Cone A 11dB Amplitude by Cohort and Eye

This figure will be similar to Figure 3.

Figure 18. Mean Change from Baseline in LA Cone A 11dB Implicit Time by Cohort and Eye

This figure will be similar to Figure 3.

Figure 19. Mean Change from Baseline in LA Flicker Amplitude by Cohort and Eye

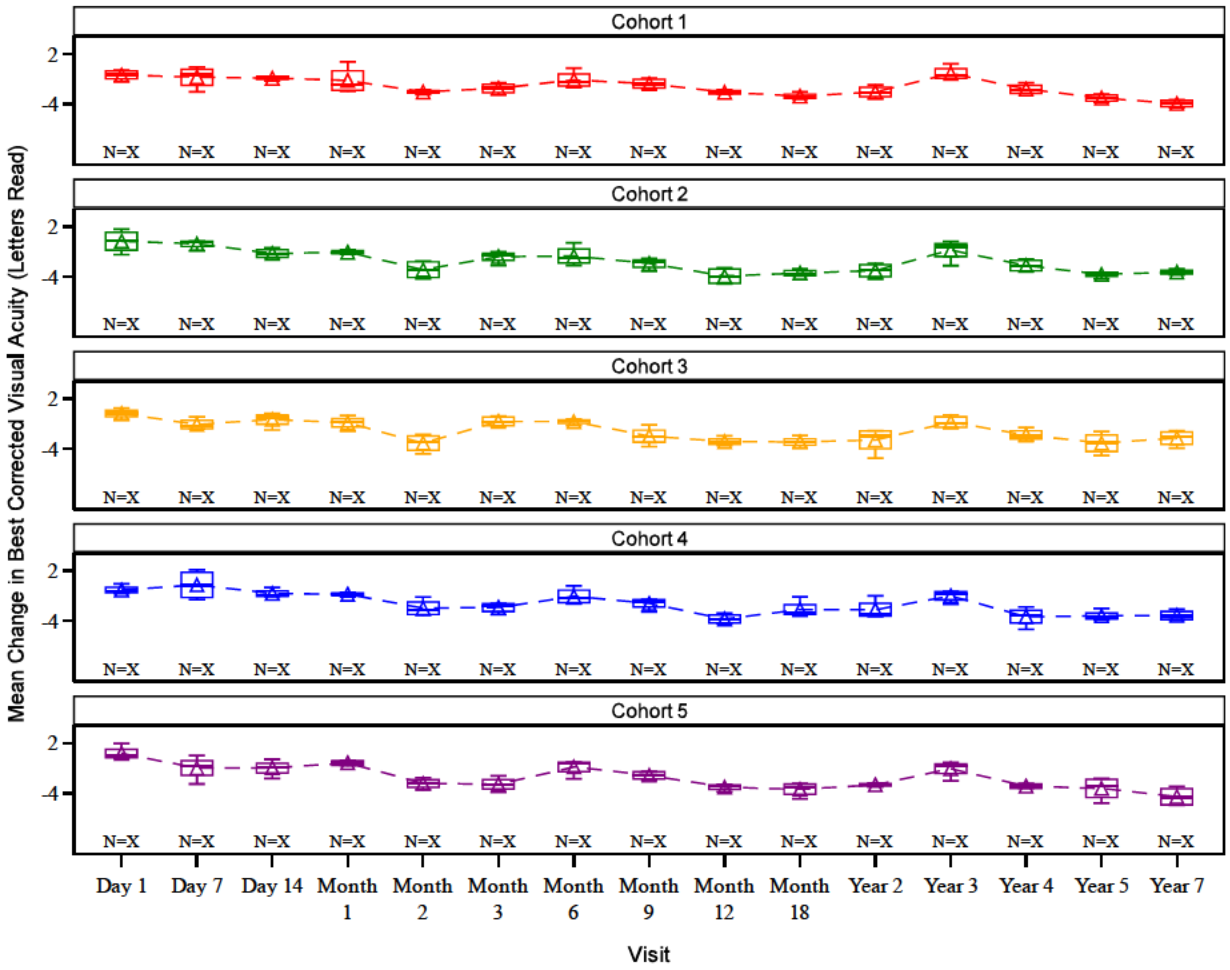
This figure will be similar to Figure 3.

Figure 20. Mean Change from Baseline in LA Flicker Implicit Time by Cohort and Eye

This figure will be similar to Figure 3.

Figure 21. Box Plot of Mean Change from Baseline in Best Corrected Visual Acuity (BCVA) as Measured by Electronic Visual Acuity (EVA) by Cohort in the Study Eye

Implementation Note: This is an example figure.



Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.

Change is computed relative to the average of the two baseline visits.

Figure 22. Box Plot of Mean Change from Baseline in Best Corrected Visual Acuity (BCVA) as Measured by Electronic Visual Acuity (EVA) by Cohort in the Fellow Eye

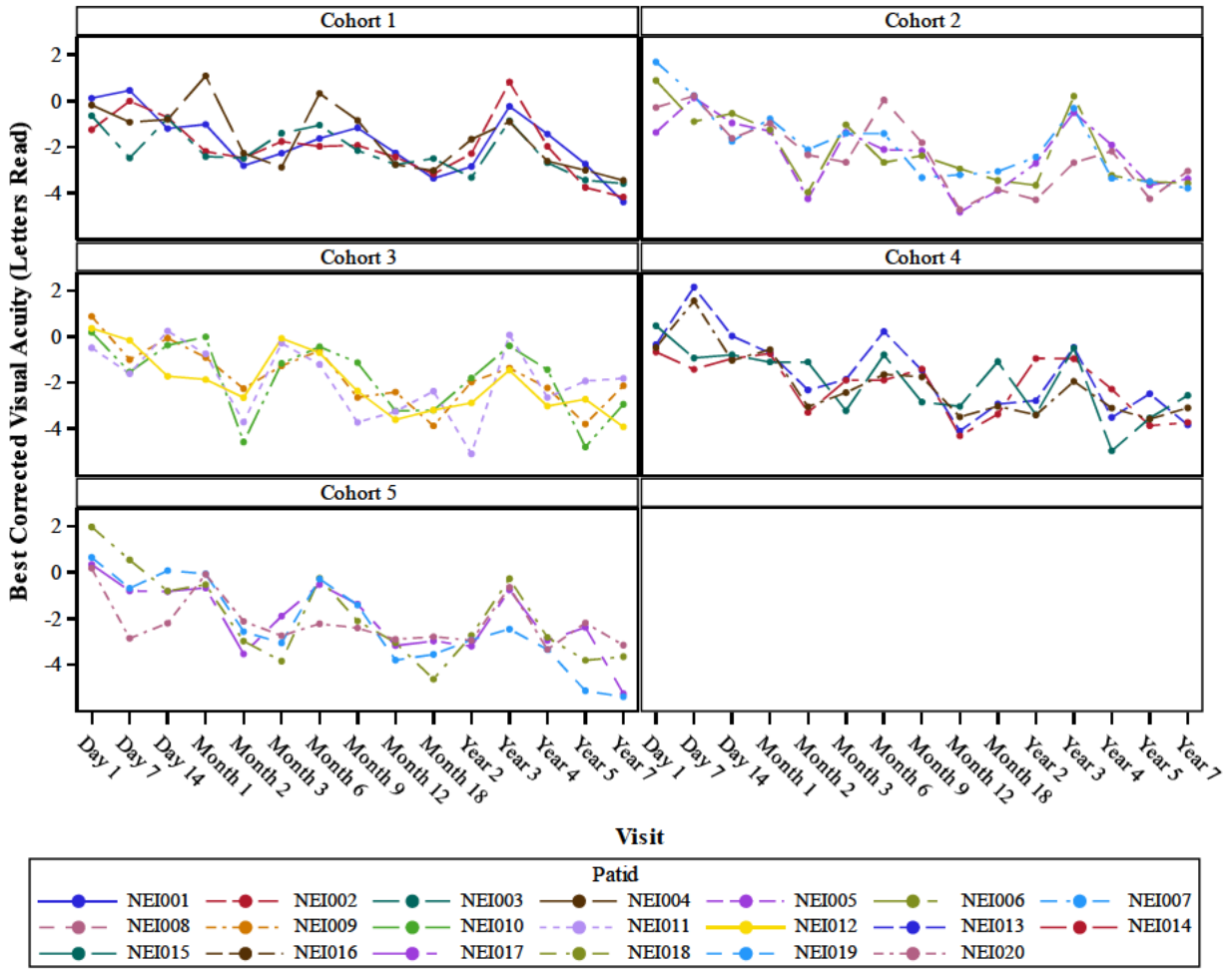
This figure will be similar to Figure 21.

Figure 23. Mean Change from Baseline in Best Corrected Visual Acuity (BCVA) as Measured by Electronic Visual Acuity (EVA) by Cohort and Eye

This figure will be similar to Figure 3.

Figure 24. Best Corrected Visual Acuity (BCVA) as Measured by Electronic Visual Acuity (EVA) Over Time in the Study Eye by Participant

Implementation Note: This is an example figure.



Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.

Figure 25. Best Corrected Visual Acuity (BCVA) as Measured by Electronic Visual Acuity (EVA) Over Time in the Fellow Eye by Participant

This figure will be similar to Figure 24.

Figure 26. Mean Change from Baseline in Intraocular Pressure (IOP) by Cohort and Eye

This figure will be similar to Figure 3.

Figure 27. Intraocular Pressure (IOP) Over Time in the Study Eye by Participant

This figure will be similar to Figure 24.

Figure 28. Intraocular Pressure (IOP) Over Time in the Fellow Eye by Participant

This figure will be similar to Figure 24.

APPENDIX 3. LISTINGS

LIST OF LISTINGS

Listing 1. Participant Early Terminations and Study Completions

Cohort	Participant ID	Date of Last Contact	Visit	Years from Injection Date[a]	Early Termination?	Early Termination Reason	Specify Other Reason[b]	Comments[b]
1	xxxxxx	xx/xx/xx	xxx	xx.x	Yes/No	xxxx	xxxx	xxxx
	xxxxxx	xx/xx/xx	xxx	xx.x	Yes/No	xxxx	xxxx	xxxx
..	xxxxxx	xx/xx/xx	xxx	xx.x	Yes/No	xxxx	xxxx	xxxx
	xxxxxx	xx/xx/xx	xxx	xx.x	Yes/No	xxxx	xxxx	xxxx

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
[a] Number of years from the injection date to the termination date. Rounded to nearest tenth.
[b] Taken verbatim as entered by site staff.

Listing 2. Participant Demographics Characteristics

Cohort	Participant ID	Registration Date	Study Eye	Age	Sex	Ethnicity	Race
1	xxxxxx	xx/xx/xx	xx	xx	xxx	xxxx	xxxx
	xxxxxx	xx/xx/xx	xx	xx	xxx	xxxx	xxxx
..	xxxxxx	xx/xx/xx	xx	xx	xxx	xxxx	xxxx
	xxxxxx	xx/xx/xx	xx	xx	xxx	xxxx	xxxx

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye.
Cohort 5 is dose group 3e11 vg/eye.

Listing 3. Medical and Ocular History

Cohort	Participant ID	Study Eye	Exam Date	Medical History[a]	Medication History (Date of last dose or vaccination)[a]	Ocular History (Eye)	Ocular Procedures (Eye: Date)[a]
1	xxxxxx	xx	xx/xx/xx	xxx	xxx: xx/xx/xx	xxxx (xx)	xx (xx: xx/xx/xx)
	xxxxxx	xx	xx/xx/xx	xxx	xxx: xx/xx/xx	xxxx (xx)	xx (xx: xx/xx/xx)
..	xxxxxx	xx	xx/xx/xx	xxx	xxx: xx/xx/xx	xxxx (xx)	xx (xx: xx/xx/xx)
	xxxxxx	xx	xx/xx/xx	xxx	xxx: xx/xx/xx	xxxx (xx)	xx (xx: xx/xx/xx)

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
[a] Dates may be included if applicable.

Listing 4. Prior and Concomitant Medications

Implementation Note: If there is no medication stop date, the duration should be listed as "Ongoing."

Cohort	Participant ID	Medication	ATC Level 1 (ATC Level 2)	Dose	Medication Start Day	Duration[a]	Indication[b]
1	xxxxxx	xx	xx	xx	xx/xx/xx	xx	xx
	xxxxxx	xx	xx	xx	xx/xx/xx	xx	xx
..	xxxxxx	xx	xx	xx	xx/xx/xx	xx	xx

Abbreviations: ATC-Anatomical Therapeutic Chemical (as classified by the World Health Organization)
[a] Duration is calculated as medication stop date – medication start date + 1.
[b] Taken verbatim as entered by site staff.

Listing 5. Investigational Product Administration

Cohort	Dose Group	Participant ID	Injection Date	Treated Eye	Injection Complications	Level of Pain at Discharge[a]
1	xxxxxx	xxxxxx	xx/xx/xx	xxx	xxxx	xxxx
1	xxxxxx	xxxxxx	xx/xx/xx	xxx	xxxx	xxxx
2	xxxxxx	xxxxxx	xx/xx/xx	xxx	xxxx	xxxx
…	xxxxxx	xxxxxx	xx/xx/xx	xxx	xxxx	xxxx

[a] Pain is subjectively reported by the participant as their level of post-injection pain at discharge from the operating room and is measured from 0 (No pain) to 10 (Intense Pain).

Listing 6. Participant Specific Protocol Deviations

Cohort	Participant ID	Departure Date	Departure Type	Departure Description[a]	Departure Outcome	Other, Specify[a]
1	xxxxxx	xx/xx/xx	xxxxxx	xxxxxx	xxxxxx	xxxxxx
		xx/xx/xx	xxxxxx	xxxxxx	xxxxxx	xxxxxx
2	xxxxxx	xx/xx/xx	xxxxxx	xxxxxx	xxxxxx	xxxxxx
…	xxxxxx	xx/xx/xx	xxxxxx	xxxxxx	xxxxxx	xxxxxx

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye.
Cohort 5 is dose group 3e11 vg/eye.
[a] Taken verbatim as entered by site staff.

Listing 7. Non-Participant Specific Protocol Deviations

Departure Date	Departure Type	Departure Description[a]	Departure Outcome	Other, Specify[a]
xx/xx/xx	xxxxxx	xxxxxx	xxxxxx	xxxxxx
xx/xx/xx	xxxxxx	xxxxxx	xxxxxx	xxxxxx
xx/xx/xx	xxxxxx	xxxxxx	xxxxxx	xxxxxx
xx/xx/xx	xxxxxx	xxxxxx	xxxxxx	xxxxxx

[a] Taken verbatim as entered by site staff.

Listing 8. Participant Specific Unanticipated Problems

Cohort	Participant ID	Problem Date	Problem Type	Problem Description[a]	Problem Outcome
1	xxxxxx	xx/xx/xx	xxxxxx	xxxxxx	xxxxxx
		xx/xx/xx	xxxxxx	xxxxxx	xxxxxx
2	xxxxxx	xx/xx/xx	xxxxxx	xxxxxx	xxxxxx
…	xxxxxx	xx/xx/xx	xxxxxx	xxxxxx	xxxxxx

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye.
Cohort 5 is dose group 3e11 vg/eye.
[a]Taken verbatim as entered by site staff.

Listing 9. Non-Participant Specific Unanticipated Problems

Problem Date	Problem Type	Problem Description[a]	Problem Outcome
xx/xx/xx	xxxxxx	xxxxxx	xxxxxx
xx/xx/xx	xxxxxx	xxxxxx	xxxxxx
xx/xx/xx	xxxxxx	xxxxxx	xxxxxx
xx/xx/xx	xxxxxx	xxxxxx	xxxxxx

[a]Taken verbatim as entered by site staff.

Listing 10. Participant Specific Non-Compliance Events

Cohort	Participant ID	Event Date	Event Type	Event Description[a]	Event Outcome
1	xxxxxx	xx/xx/xx	xxxxxx	xxxxxx	xxxxxx
		xx/xx/xx	xxxxxx	xxxxxx	xxxxxx
2	xxxxxx	xx/xx/xx	xxxxxx	xxxxxx	xxxxxx
…	xxxxxx	xx/xx/xx	xxxxxx	xxxxxx	xxxxxx

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye.
Cohort 5 is dose group 3e11 vg/eye.
[a]Taken verbatim as entered by site staff.

Listing 11. Non-Participant Specific Non-Compliance Events

Event Date	Event Type	Event Description[a]	Event Outcome
xx/xx/xx	xxxxxx	xxxxxx	xxxxxx
xx/xx/xx	xxxxxx	xxxxxx	xxxxxx
xx/xx/xx	xxxxxx	xxxxxx	xxxxxx
xx/xx/xx	xxxxxx	xxxxxx	xxxxxx

[a]Taken verbatim as entered by site staff.

Listing 12. Suspension Rule Assessment

				Decrease in Visual Function[a]								
Cohort	Participant ID	Visit	Exam Date	VA[b]	ERG Amplitude[c]	Endoph.	ACC Reaction[d]	Vitreous Cells Reaction[e]	Optic Nerve Edema[f]	Retinitis[g]	Systemic Response[h]	SAE (MedDRA PT)[i]
1	XXXXXX	Day 1	xx/xx/xx	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No (xx)
		Day 7	xx/xx/xx	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No (xx)
…	XXXXXX	…	xx/xx/xx	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No (xx)

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
Abbreviations: ACC-Anterior Chamber Cell; Endoph- Endophthalmitis**;** ERG-Electroretinogram; PT-Preferred Term; SAE-Serious Adverse Event; VA-Visual Acuity
Ophthalmic occurrences are assessed for the study eye. Baseline values are the average of the two baseline visits.
[a] A significant decrease in visual function, unless this decline is attributable to ocular surface effects or due to minimal inflammation (anterior chamber pigmented or nonpigmented cells of grade 1+ or less) from the intravitreal injection procedure during the first 10 days following administration of the investigational product
[b] Decrease in best corrected visual acuity of ≥ 10 Early Treatment Diabetic Retinopathy Study letters
[c] Decrease in ERG response amplitude (DA Rod, DA Comb A 0dB, DA Comb B 0dB, DA Comb A 11dB, DA Comb B 11dB, DA O.P.s, LA Cone B 0dB, LA Cone A 11dB, LA Flicker) ≥ 75%
[d] Anterior chamber cellular reaction of Grade 3+ or higher
[e] Vitreous cellular reaction of Grade 3+ or higher In any portion of the vitreous cavity
f Optic nerve edema of Grade 1+ or higher
[g] Retinitis, retinal vasculitis, or choroiditis
[h] As reflected by Grade 2 lab test or any Grade 3-4 event/laboratory test related to the investigational product
[i] SAE related to the study article

Listing 13. Adverse Events

Cohort	Participant ID	Event Date	Study Day[a]	Reporting Period[b]	MedDRA PT[c]	Eye	Intervention	Specify[d]	Inpatient Care	Outcome	Duration (Days)[e]	Effect on IP	Related to Procedure[f]	Related to IP	Severity	SAE
x	xxxxxx	xx/xx/xx	xx	xx	xxxxxx	xxxx	xxxx	xxxx	xx	xxxxxx	xx	xxxx	xx	xx	xxxx	xx
		xx/xx/xx	xx	xx	xxxxxx	xxxx	xxxx	xxxx	xx	xxxxxx	xx	xxxx	xx	xx	xxxx	xx
		xx/xx/xx	xx	xx	xxxxxx	xxxx	xxxx	xxxx	xx	xxxxxx	xx	xxxx	xx	xx	xxxxx	xx

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
Abbreviations: IP-Investigational Product; PT-Preferred Term; SAE-Serious Adverse Event
[a] Study day is calculated as event date - IP injection date + 1
[b] Categorized as I (Immediate Safety Follow-Up: Day 0 [injection day, within 24 hours] through Day 7, inclusive of both these dates), EPS (Early Post-Surgery Safety Follow-Up: Day 8 through Year 2, inclusive); LT (Long-Term Safety Follow-Up: Year 2 through end of study participant)
[b] MedDRA Version XX
[c] Taken verbatim as entered by site staff.
[d] Duration is total number of days elapsed from the event date to resolution date + 1
[e] Surgical procedure

Listing 14. Serious Adverse Events

This listing will be similar to Listing 22 without the SAE column.

Listing 15. Natural Progression of Disease

Cohort	Participant ID	Study Eye	Event Date	Description[a]	MedDRA Preferred Term[b]
x	**xxxxxx**	xx	xx/xx/xx	xxxxxxx	xxxxxxx
			xx/xx/xx	xxxxxxx	xxxxxxx
			xx/xx/xx	xxxxxxx	xxxxxxx

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
[a] Taken verbatim as entered by site staff
[b] MedDRA Version XX

Listing 16. Primary Outcome of Ocular and Systemic Safety Events

Implementation Note: If no event occurred for the given visit, the response should be "No." If an event did occur, details of the events will be provided; for example, a decrease of 11 letters will be captured as "11 letters" and a decrease in ERG response amplitude for DA Rod of 80% will be captured as "DA Rod, 80%."

Cohort	Participant ID	Visit	Date	VA Decrease[a]	ERG Decrease[b]	Severe Ocular Inflammation[c]	Clinically Related AE (MedDRA PT)[d]	Abnormal Lab Finding[e]
1	NEI001	Day 1	xx/xx/xx	xx	xx	xx	xx	xx
		Day 7	xx/xx/xx	xx	xx	xx	xx	xx
		NA						
…								

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
Abbreviations: AE-Adverse Event; ERG-Electroretinogram; PT-Preferred Term; VA-Visual Acuity
[a] Decrease in best corrected visual acuity of ≥ 10 electronic visual acuity letters in the study eye
[b] Decrease in ERG response amplitude (DA Rod, DA Comb A 0dB, DA Comb B 0dB, DA Comb A 11dB, DA Comb B 11dB, DA O.P.s, LA Cone B 0dB, LA Cone A 11dB, LA Flicker) ≥ 75% in the study eye
[c] Beyond inflammation anticipated consequent to an intravitreal injection and occurring in the study eye.
[d] Includes vitreous hemorrhage, retinal detachment, intraocular pressure elevation, lens damage and endophthalmitis occurring in the study eye.
[e] Must be beyond Grade 1 (Common Terminology Criteria for Adverse Events [CTCAE] 5.0) and/or clinically significantly different than baseline regardless of potential relationship to the AAV vector.

Listing 17. DA Rod

			DA Rod							
			Study Eye				Fellow Eye			
Cohort	**Participant ID**	**Visit**	**Amp (µV)**	**Amp Δ (µV)**	**Imp (ms)**	**Imp Δ (ms)**	**Amp (µV)**	**Amp Δ (µV)**	**Imp (ms)**	**Imp Δ (ms)**
1	**xxxxxx**	Day 1	xx	xx	xx	xx	xx	xx	xx	xx
		…	xx	xx	xx	xx	xx	xx	xx	xx

Abbreviations: Amp-amplitude; Imp-implicit time
Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye.
Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
Baseline response is the average of the two baseline visits. Δ indicates change from baseline.

Listing 18. DA Comb 0dB

This listing will be similar to Listing 17 but will include both DA Comb A 0db and DA Comb B 0dB values.

Listing 19. DA Comb 11dB

This listing will be similar to Listing 17 but will include both DA Comb A 11db and DA Comb B 11dB values.

Listing 20. DA O.P.s

This listing will be similar to Listing 17.

Listing 21. LA Cone

This listing will be similar to Listing 17 but will include both LA Cone B 0db and LA Cone A 11dB values.

Listing 22. LA Flicker

This listing will be similar to Listing 17.

Listing 23. Best Corrected Visual Acuity (BCVA) as Measured by Electronic Visual Acuity (EVA)

		Baseline BCVA (letters read)			BCVA (letters read)		BCVA Δ (letters read)	
Cohort	**Participant ID**	**Study Eye**	**Fellow Eye**	**Visit**	**Study Eye**	**Fellow Eye**	**Study Eye**	**Fellow Eye**
x	xxxxxx	xx	xx	Day 1	xx	xx	xx	xx
				Day 7	xx	xx	xx	xx
				Day 14	xx	xx	xx	xx
				…	xx	xx	xx	xx

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
If manifest refraction is done then total letters read is based on manifest refraction; if manifest refraction is not done then total letters read is based on last manifest refraction.
Baseline response is the average of the two baseline visits. Δ indicates change from baseline.
*Indicates visual acuity was determined via manifest refraction.

Listing 24. Best Corrected Visual Acuity (BCVA) as Measured by Early Treatment Diabetic Retinopathy Study (ETDRS)

This listing will be similar to Listing 23.

Listing 25. Completion of Optical Coherence Tomography (OCT) Imaging

			OCT Completed	
Cohort	**Participant ID**	**Visit**	**Study Eye**	**Fellow Eye**
x	xxxxxx	Baseline 1	Yes/No	Yes/No
		Baseline 2	Yes/No	Yes/No
		Day 14	Yes/No	Yes/No
		…	Yes/No	Yes/No

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.

Listing 26. Completion of Microperimetry (MP-1) Imaging

This listing will be similar to Listing 25.

Listing 27. Immunosuppressive (Prednisone, Cyclosporine, and Mycophenolate) Regimen

Participant ID	Medication Name	Start Date	Start Dose	Start Dose Days from Injection	Actual Date 1	Actual Dose 1	Dose 1 Days from Injection	Actual Date 2	Actual Dose 2	Dose 2 Days from Injection	Actual Date 3	Actual Dose 3	Dose 3 Days from Injection	Actual Date 4
xxxxxx	<Medication 1>	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx
	<Medication 1>	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx
…	…													

Actual Dose 4	Dose 4 Days from Injection	Actual Date 5	Actual Dose 5	Dose 5 Days from Injection	Actual Date 6	Actual Dose 6	Dose 6 Days from Injection	Actual Date 7	Actual Dose 7	Dose 7 Days from Injection	Actual Date 8	Actual Dose 8	Dose 8 Days from Injection	Actual Date 9	Actual Dose 9
xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx
xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx
…	…														

Listing 27. Immunosuppressive (Prednisone, Cyclosporine, and Mycophenolate) Regimen (continued)

Dose 9 Days from Injection	Actual Date 10	Actual Dose 10	Dose 10 Days from Injection	Actual Date 11	Actual Dose 11	Dose 11 Days from Injection	Actual Date 12	Actual Dose 12	Dose 12 Days from Injection	Actual Date 13	Actual Dose 13	Dose 13 Days from Injection	Actual Date 14	Actual Dose 14	Dose 14 Days from Injection
xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx
xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx
…	…														

Actual Date 15	Actual Dose 15	Dose 15 Days from Injection	Actual Date 16	Actual Dose 16	Dose 16 Days from Injection	Actual Date 17	Actual Dose 17	Dose 17 Days from Injection	Actual Date 18	Actual Dose 18	Dose 18 Days from Injection	Actual Date 19	Actual Dose 19	Dose 19 Days from Injection
xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx
xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx	xx/xx/xx	xx	xx
…	…													

Listing 28. Ozurdex or Triesence Injection

Cohort	Participant ID	Visit	Visit Date	Ozurdex or Triesence Injection Done	Medication Used	Any Complications	Complications, Specify[a]
1	xxxxxx	xxxxxx	xx/xx/xx	xx	xxx	xxxx	xxxx
1	xxxxxx	xxxxxx	xx/xx/xx	xx	xxx	xxxx	xxxx
2	xxxxxx	xxxxxx	xx/xx/xx	xx	xxx	xxxx	xxxx
…	xxxxxx	xxxxxx	xx/xx/xx	xx	xxx	xxxx	xxxx

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye.
Cohort 5 is dose group 3e11 vg/eye.
The immunosuppressive regimen was modified to remove the oral immunosuppressive regimen and include an Ozurdex or Triesence injection with Amendment Q (Institutional Review Board approved on February 1, 2019). The first partcipant enrolled under Amendment Q was Participant NEI012.
[a] Taken verbatim as entered by site staff.

Listing 29. Anterior Chamber Tap

Cohort	Participant ID	Visit	Visit Date	AC Tap Done	Complications?	Complications, Specify[a]	Reason Not Done[a]
x	**xxxxxx**	xxxxx	xx/xx/xx	xxxxxx	xxxxxx	xxxxxx	xxxxxx
		xxxxx	xx/xx/xx	xxxxxx	xxxxxx	xxxxxx	xxxxxx
		xxxxx	xx/xx/xx	xxxxxx	xxxxxx	xxxxxx	xxxxxx

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye.
Cohort 5 is dose group 3e11 vg/eye.
[a] Taken verbatim as entered by site staff.

Listing 30. Intraocular Pressure (IOP)

This listing will be similar to Listing 23.

Listing 31. Laboratory Assessments

Cohort	Participant ID	Visit	Exam Date	Abnormal Lab(s)	Specify[a]	Change from Baseline	Clinically Significant	Specify[a]
x	**xxxxxx**	Baseline 1	xx/xx/xx	Yes/No	xxxxxxxxxx			
		Day 7	xx/xx/xx	Yes/No	xxxxxxxxxx	Yes/No	Yes/No	xxxxxxxxxx
		…	xx/xx/xx	Yes/No	xxxxxxxxxx	Yes/No	Yes/No	xxxxxxxxxx
		Baseline 1	xx/xx/xx	Yes/No	xxxxxxxxxx			
		Day 7	xx/xx/xx	Yes/No	xxxxxxxxxx	Yes/No	Yes/No	xxxxxxxxxx
		….	xx/xx/xx	Yes/No	xxxxxxxxxx	Yes/No	Yes/No	xxxxxxxxxx

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
Labs are presented only for visits where labs are done.
[a] Taken verbatim as entered by site staff.

Listing 32. Abnormal Laboratory Assessments

Cohort	Participant ID	Visit	Laboratory Name[a]	Laboratory Value	Laboratory Units	Adverse Event	CTCAE(v5) Grade
x	**xxxxxx**	Baseline 1	xxxxxx	xx	xx	xx	xx
			xxxxxx	xx	xx	xx	xx
		….	xxxxxx	xx	xx	xx	xx
			xxxxxx	xx	xx	xx	xx
			xxxxxx	xx	xx	xx	xx
x	**xxxxxx**	Baseline 1	xxxxxx	xx	xx	xx	xx
			xxxxxx	xx	xx	xx	xx
		….	xxxxxx	xx	xx	xx	xx
			xxxxxx	xx	xx	xx	xx
			xxxxxx	xx	xx	xx	xx

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye.
Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
[a]Taken verbatim as entered by site staff.

Listing 33. Additional Ophthalmic Assessments

				Anterior Chamber				Vitreous									
				Cells		Flare		Cells		Haze		Optic Nerve Edema		Weiss Ring Present		Vitreous Separation[a]	
Cohort	Participant ID	Visit	Examination Date	Study Eye	Fellow Eye	Study Eye	Fellow Eye	Study Eye	Fellow Eye	Study Eye	Fellow Eye	Study Eye	Fellow Eye	Study Eye	Fellow Eye	Study Eye	Fellow Eye
x	xxxxxx	Baseline 1	xx/xx/xx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx
		Day 7	xx/xx/xx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx
		…	xx/xx/xx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx
x	xxxxxx	Baseline 1	xx/xx/xx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx
		Day 7	xx/xx/xx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx
		…	xx/xx/xx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx	xxxxx

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye.
Cohort 4 is dose group 1e11 vg/eye. Cohort 5 is dose group 3e11 vg/eye.
Red highlighting corresponds to Grade 3 or higher anterior chamber cells; Grade 3 or higher vitreous cells; or optic nerve edema 1-5 stages.
[a] Optical coherence tomography shows posterior vitreous separation

Listing 34. Telephone Follow-up Assessments

Cohort	Participant ID	Visit	Visit Date	New Procedures?[a]	Malignancies Diagnosed?	Hematological Events?	Autoimmune Events?	Significant Ocular Changes?
x	**xxxxxx**	Year 6	xx/xx/xx	xxxx	xxxx	xxxx	xxxx	xxxx
		Year 7	xx/xx/xx	xxxx	xxxx	xxxx	xxxx	xxxx
		…	xx/xx/xx	xxxx	xxxx	xxxx	xxxx	xxxx
x	**xxxxxx**	Year 6	xx/xx/xx	xxxx	xxxx	xxxx	xxxx	xxxx
		Year 7	xx/xx/xx	xxxx	xxxx	xxxx	xxxx	xxxx
		…	xx/xx/xx	xxxx	xxxx	xxxx	xxxx	xxxx

Cohort 1 is dose group 1e9 vg/eye. Cohort 2 is dose group 1e10 vg/eye. Cohort 3 is dose group 1e11 vg/eye. Cohort 4 is dose group 1e11 vg/eye.
Cohort 5 is dose group 3e11 vg/eye.
[a] If any new procedures, description is taken verbatim as entered by site staff.