

Statistical Analysis Plan (SAP) Cover Page

Protocol Title: A Phase 1/2 Dose Escalation Study of Subretinally Injected ATSN-101
Administered in Patients with Leber Congenital Amaurosis Caused by Biallelic Mutations in
GUCY2D

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Atsena Therapeutics, Inc.

STATISTICAL ANALYSIS PLAN
for
Protocol: ATSN-101-1 (Previously DFI14738)

Study Title:

**A Phase 1/2 Dose Escalation Study of
Subretinally Injected ATSN-101 Administered in
Patients with Leber Congenital Amaurosis
Caused by Biallelic Mutations in *GUCY2D***

Version 2.0

DATE: 08 January 2024

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STUDY INFORMATION

Study Title	A Phase 1/2 Dose Escalation Study of Subretinally Injected ATSN-101 Administered in Patients with Leber Congenital Amaurosis Caused by Biallelic Mutations in <i>GUCY2D</i>
Study Number:	ATSN-101-1
Protocol Version:	Protocol Amendment 08
Development Phase:	Phase 1/2
Investigational Medicinal Product:	AAV5- <i>GUCY2D</i> gene therapy (ATSN-101 (previously referred to as SAR439483))
Route:	Subretinal injection in the central retina
Indication Studied:	Leber Congenital Amaurosis Cased by Biallelic Mutations in <i>GUCY2D</i>
Sponsor:	Atsena Therapeutics, Inc.
Date of the Analysis Plan:	08 January 2024
Version Number:	2.0

VERSION HISTORY

SAP Version	Approval Date	Change	Rationale
1.0	20-JUN-2023	Not Applicable	Original version.
2.0	08-JAN-2024	<p>Study number changed from DFI14738 to ATSN-101-1.</p> <p>Study compound changed from SAR439483 to ATSN-101.</p> <p>Updated Sections 4. – 6. And Appendices 2 – 4 based on Protocol amendment 08 and discussions with Sponsor.</p> <p>Added appendix 5 to provide ICH E3 numbering to the SAP tables, figures and listings.</p>	Protocol amendment 08

SIGNATURE PAGE

SPONSOR: Atsena Therapeutics, Inc.

STUDY TITLE: A Phase 1/2 Dose Escalation Study of Subretinally Injected ATSN-101 Administered in Patients with Leber Congenital Amaurosis Caused by Biallelic Mutations in *GUCY2D*

STUDY NUMBER: ATSN-101-1 (previously DFI14738)

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TABLE OF CONTENTS

STUDY INFORMATION	II
VERSION HISTORY	III
TABLE OF CONTENTS.....	V
LIST OF ABBREVIATIONS.....	VIII
1. INTRODUCTION	1
1.1. Purpose and Structure of the Document	1
1.2. Purpose of the Analyses.....	1
1.3. Timing of the Final Analyses.....	1
2. INVESTIGATIONAL PLAN.....	2
2.1. Overall Study Design and Plan	2
2.2. Data Monitoring Committee	2
2.3. Study Objectives and Endpoints	3
2.3.1. Study Objectives	3
2.3.2. Study Endpoints	3
2.4. Study Flow Chart	4
2.5. Statistical Considerations for the Study Design.....	4
2.5.1. Sample Size Considerations.....	4
2.5.2. Replacement of Subjects.....	4
3. GENERAL STATISTICAL CONSIDERATIONS.....	5
3.1. Data Source	5
3.2. General Analysis Specifications	5
3.2.1. Global Analysis Principles.....	5
3.2.2. Reporting Conventions	5
3.2.3. Analysis Software and Other Technical Details	7
3.3. Analysis Populations.....	7
3.3.1. Study Periods	7
3.4. Handling of Missing Data	8
4. SUMMARY OF STUDY CONDUCT AND SUBJECTS	9
4.1. Disposition of Subjects	9

TABLE OF CONTENTS (CONTINUED)

4.2.	Subject Demographic Characteristics, Medical History and Diagnoses	9
4.3.	Extent of Study Treatment Exposure and Compliance	9
4.4.	Prior/Concomitant Medication/Therapy	9
4.5.	Protocol Deviations	9
5.	ANALYSIS OF SAFETY DATA	10
5.1.	Analysis of Primary Endpoint	10
5.1.1.	Adverse Events	10
5.1.1.1.	Treatment-emergent Adverse Events	10
5.1.1.2.	Deaths and Serious Adverse Events	10
5.1.1.3.	Adverse Events Leading to Treatment Discontinuation	11
5.1.1.4.	Adverse Events of Special Interest	11
5.1.2.	Ophthalmological Safety Endpoints	11
5.1.2.1.	Slit Lamp Examination	11
5.1.2.2.	Ophthalmoscopy	11
5.1.2.3.	Intraocular Pressure	13
5.1.2.4.	Fundus Photography	13
5.1.3.	Clinical Laboratory Evaluations	13
5.1.4.	Immunogenicity	13
5.1.5.	Vital Signs	15
5.2.	Additional Safety Analysis	15
5.2.1.	Adverse Events (AEs)	15
6.	ANALYSIS OF EFFICACY DATA	16
6.1.	Analysis of Secondary Efficacy Endpoints	16
6.1.1.	Full-field Stimulus Testing	17
6.1.1.1.	Decibels	17
6.1.1.2.	Log Units	18
6.1.2.	Best-Corrected Visual Acuity	18
6.2.	Analysis of Exploratory Endpoints	19
6.2.1.	Pupillometry	19
6.2.1.1.	University of Pennsylvania Site	19

TABLE OF CONTENTS (CONTINUED)

6.2.1.2. Oregon Health and Science University Site	20
6.2.2. Oculomotor Instability	21
6.2.3. Photoaversion.....	21
6.2.4. Low-luminance Visual Acuity	21
6.2.5. Optical Coherence Tomography	21
6.2.5.1. EDC Data.....	22
6.2.5.2. MERIT Data	22
6.2.6. Visual Function Questionnaire	22
6.2.7. Patient's Experience Due to Changes in Vision Questionnaire.....	23
6.2.8. Mobility Testing.....	23
7. INTERIM ANALYSES	24
8. SUMMARY OF CHANGES TO THE CONDUCT OF THE STUDY AND PLANNED ANALYSES.....	25
9. QUALITY ASSURANCE	26
10. REFERENCES	27
APPENDICES	28
APPENDIX 1. POTENTIALLY CLINICALLY SIGNIFICANT ABNORMALITIES CRITERIA	29
APPENDIX 2. TABLES	31
APPENDIX 3. FIGURES	81
APPENDIX 4. LISTINGS	98
APPENDIX 5. ICH E3 NUMBERING.....	125

LIST OF ABBREVIATIONS

ADA	Anti-Drug Antibodies
AE	Adverse Event
AESI	Adverse Event of Special Interest
ANOVA	Analysis of Variance
ATC	Anatomical Therapeutic Chemical
BCVA	Best-Corrected Visual Acuity
BMI	Body Mass Index
BP	Blood Pressure
BRVT	Berkeley Rudimentary Vision Test
CHOP	Children's Hospital of Philadelphia
CME	Cystoid Macular Edema
CSR	Clinical Study Report
CV	Coefficient of Variation
CVAQC	Cardiff Visual Ability Questionnaire for Children
dB	Decibels
DBP	Diastolic Blood Pressure
DMC	Data Monitoring Committee
EDC	Electronic Data Capture
ELM	External Limiting Membrane
ETDRS	Early Treatment Diabetic Retinopathy Study
EZ	Ellipsoid Zone
FDA	Food and Drug Administration
FST	Full-Field Stimulus Testing
GEE	Generalized Estimating Equation
GUCY2D	Guanylate Cyclase 2D
HLGT	High Level Group Term
HLT	High Level Term
HR	Heart Rate
ICH	International Conference on Harmonization

LIST OF ABBREVIATIONS (CONTINUED)

IMP	Investigational Medicinal Product
IOP	Intraocular Pressure
IQR	Interquartile Range
IS/OS	Inner Segment/Outer Segment
LCA	Leber Congenital Amaurosis
LLVA	Low-luminance Visual Acuity
MAD	Maximum Administered Dose
mL	Milliliter
MLMT	Multi-Luminance Mobility Testing
mm	Millimeter
ms	Millisecond
MTD	Maximum Tolerated Dose
NEI VFQ	National Eye Institute Visual Function Questionnaire
NIMP	Non-Investigational Medicinal Product
OCI	Oculomotor Instability
OCT	Optical Coherence Tomography
OHSU	Oregon Health and Science University
ONL	Outer Nuclear Layer
OS	Outer Segment
PCSA	Potentially Clinically Significant Abnormality
PECV	Patient's Experience Due to Changes in Vision
PT	Preferred Term
RPE	Retinal Pigment Epithelium
s	Seconds
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SBP	Systolic Blood Pressure
SD	Standard Deviation
SD-OCT	Spectral Domain Optical Coherence Tomography
SE	Standard Error

LIST OF ABBREVIATIONS (CONTINUED)

SOC	System Organ Class
TEAE	Treatment-Emergent Adverse Event
TFLs	Tables, Figures and Listings
TPLR	Transient Pupillary Light Reflex
UPenn	University of Pennsylvania
vg	Vector Genomes

1. INTRODUCTION

1.1. Purpose and Structure of the Document

The Statistical Analysis Plan (SAP) for “A Phase 1/2 Dose Escalation Study of Subretinally Injected ATSN-101 Administered in Patients with Leber Congenital Amaurosis Caused by Biallelic Mutations in *GUCY2D*” (Protocol ATSN-101-1) describes and expands upon the statistical information presented in the protocol.

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 Conferences on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) 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 for statistical practice.

This document contains five sections: (1) a description of the purpose and timing of analyses; (2) a description of the study design, objectives, and the variables collected/assessed to be used in analyses; (3) general statistical principles; (4) comprehensive statistical analysis methods for study outcomes; (5) a list of proposed tables, figures, and listings (TFLs) with mock-ups (Appendices 2, 3, and 4) and (6) a list of ICH E3 numbering for the SAP TFL numbers (Appendix 5). Any deviations from this SAP will be described and justified in protocol amendments and/or in the CSR, as appropriate. The reader of this SAP is encouraged to also review the study protocol for details on conduct of the study and the operational aspects of clinical assessments.

1.2. Purpose of the Analyses

These analyses will assess the safety, tolerability, and efficacy of ascending doses of ATSN-101 administered as a unilateral subretinal injection in subjects with Leber Congenital Amaurosis (LCA) caused by autosomal recessive *GUCY2D* mutations (*GUCY2D*-LCA).

1.3. Timing of the Final Analyses

The final analysis will be performed after study completion at Week 260 when all data have been entered, all data queries have been resolved, and the database has been locked.

2. INVESTIGATIONAL PLAN

2.1. Overall Study Design and Plan

ATSN-101-1 is a Phase 1/2, multi-center, open-label, unilateral (one eye) study of subretinally injected ATSN-101. The study is separated into two parts including a dose escalation phase (Part A) and a dose expansion phase (Part B).

The dose escalation phase (Part A) will evaluate three ascending dose levels of ATSN-101 in three successive cohorts (Cohorts 1-3). A total of approximately nine subjects ≥ 18 years of age (three subjects per cohort) are planned, though up to 15 may be included based on needs for additional cohorts at intermediate doses or to replicate dose levels. For Cohort 1 of the dose escalation phase, there will be an interval of at least 14 days between dosing of each of the three subjects that will be observed in order to assess safety. For the remaining dose escalation cohorts (Cohorts 2 and 3), there will be an interval of at least 14 days between dosing the first and second subject and an interval of at least seven days between dosing the second and third subject that will be observed in order to assess safety.

The dose expansion phase (Part B) will include two cohorts, both treated at the maximum tolerated dose (MTD) or maximum administered dose (MAD), determined from Part A. These two cohorts will enable further characterization of the risk benefit profile of ATSN-101 in the adult (Cohort 4) and pediatric (Cohort 5) populations. Cohort 4 will include approximately three subjects ≥ 18 years of age and Cohort 5 will include approximately three subjects ≥ 6 years of age and < 18 years of age. Cohorts 4 and 5 will be enrolled simultaneously. For Cohort 4, there will be an interval of at least seven days between dosing each subject that will be observed to assess safety. For Cohort 5, there will be an interval of at least 14 days between dosing of each of the three subjects that will be observed to assess safety.

The Screening and Baseline period will be up to 56 days, the duration of the Main Study Period will be approximately 52 weeks, and the Extension Study Period will include an additional 208 weeks, for a total post-treatment study duration of approximately 260 weeks and a total study duration, including Screening and Baseline, of up to 268 weeks.

2.2. Data Monitoring Committee

An independent Data Monitoring Committee (DMC) will be convened to monitor safety and will meet regularly either at face-to-face meetings or by teleconference. The Committee will review the available safety data for each individual subject, and make recommendations regarding dose escalation, study continuance and study conduct.

At least 14 days of safety data will be reviewed by the DMC for each cohort prior to dose escalation.

The DMC will also review at least 14 days of safety data post treatment from the final dose escalation cohort in Part A prior to enrolling Part B.

New cohorts will be initiated only after agreement by the Sponsor and DMC that the safety and tolerability demonstrated in prior cohorts support further dosing.

Before enrolling Cohort 5, a preliminary summary of safety and biological activity data of Part A along with a rationale for the dose to be used in Cohort 5 will be provided to the DMC for review. This information will also be submitted to the Regulatory Authorities and other review committees as required by local site requirements.

The DMC will meet at least once more after the completion of the Main Study Period of the last subject to monitor safety.

Furthermore, the DMC will review events triggering study stopping rules as defined in Section 5.2.6.2 of the protocol.

2.3. Study Objectives and Endpoints

2.3.1. Study Objectives

Primary Objective

To evaluate the safety and tolerability of ascending doses of ATSN-101 administered as a unilateral subretinal injection in subjects with *GUCY2D*-LCA.

Secondary Objective

To evaluate the efficacy of ascending doses of ATSN-101 administered as a unilateral subretinal injection in subjects with *GUCY2D*-LCA.

2.3.2. Study Endpoints

Primary Endpoint

The incidence of adverse events (AEs, serious adverse events [SAEs], adverse events of special interest [AESIs]) over a 52-week period following a single subretinal dose of ATSN-101. Clinically significant changes from baseline in safety assessments will be noted.

Secondary (Efficacy) Endpoints

- Full-field stimulus testing (FST)
- Best-corrected visual acuity (BCVA)

Exploratory Endpoints

- Pupillometry
- Oculomotor instability (OCI)
- Photoaversion
- Low-luminance visual acuity (LLVA)
- Optical coherence tomography (OCT)
- Visual Function Questionnaire (Note: National Eye Institute Visual Function Questionnaire-25 [NEI VFQ-25] will be used for Cohorts 1-4; The Cardiff Ability Questionnaire for Children [CVAQC] will be used for Cohort 5)
- Patient's Experience due to Changes in Vision (PECV) Questionnaire
- Mobility testing (Note: Mobility testing will be performed on subjects at sites where testing is available.)

2.4. Study Flow Chart

The study flow chart is included in Section 2.2 of the protocol.

2.5. Statistical Considerations for the Study Design

2.5.1. Sample Size Considerations

This is a Phase 1/2 dose escalation study. No formal sample size calculation has been performed.

Cohorts of approximately three subjects will be screened and treated at the same dose level during the Dose Escalation phase in three dose levels (1.0×10^{10} vector genomes/eye [vg/eye], 3.0×10^{10} vg/eye, and 1.0×10^{11} vg/eye). The actual number of dose levels examined and the emerging ATSN-101 related toxicities will determine the total sample size during the Dose Escalation phase.

It is anticipated that approximately nine subjects, but up to 15 based on needs for additional cohorts at intermediate doses or to replicate dose levels, will be required to establish the MTD of ATSN-101. Approximately three subjects may be enrolled in Cohort 4, and approximately three subjects may be enrolled in Cohort 5. The goal is to have a total of approximately 15 evaluable subjects treated.

2.5.2. Replacement of Subjects

Subjects withdrawing from follow-up monitoring before the primary endpoint has been established at 52 weeks after administration of ATSN-101 may be replaced in order to have three evaluable subjects per cohort. More than three subjects may be enrolled per cohort to accommodate replacement or to gain additional experience. Decisions regarding replacement will be made by the Sponsor. However, in the case of discontinuation related to an AE, the replacement will be discussed between the Investigator and the Sponsor.

3. GENERAL STATISTICAL CONSIDERATIONS

3.1. Data Source

Data are being captured/analyzed by multiple sources – electronic data capture (EDC) via eClinical Solutions, MERIT Inc., Children’s Hospital of Philadelphia (CHOP), and ORA Inc.

Data for the following ocular assessments are being collected as follows. All other data are being captured in EDC.

	University of Pennsylvania (UPenn)					Oregon Health and Science University (OHSU)	
	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 4	Cohort 5
BCVA	EDC	EDC	EDC	EDC	EDC	EDC	EDC
LLVA^a	EDC	EDC	EDC	EDC	EDC	EDC	EDC
FST	EDC	EDC	EDC	EDC	EDC	EDC	EDC
OCT	EDC	EDC	09 and 010: EDC 012: MERIT ^b	MERIT ^b	MERIT ^b	MERIT ^b	MERIT ^b
OCI	EDC	EDC	09 and 010: EDC 012: MERIT ^b	MERIT ^b	MERIT ^b	MERIT ^b	MERIT ^b
Pupillometry	EDC	EDC	EDC	EDC	EDC	MERIT	MERIT
Photoaversion	EDC	EDC	EDC	EDC	EDC	EDC	EDC
Mobility Testing	CHOP	CHOP	CHOP	CHOP	CHOP	ORA ^c	ORA ^c
^a LLVA data for the UPenn site will not be provided to the Coordinating Center for statistical analysis. ^b Subject 012 (Cohort 3) and all Cohort 4 and 5 subjects were recruited under Amendment 5 or later and will be analyzed at MERIT. ^c Mobility testing data from ORA Inc. will not be provided to the Coordinating Center for statistical analysis.							

Separate analyses will be performed for OCT, pupillometry, and mobility testing where data are being provided by more than one source. OCI data from EDC and MERIT can be analyzed together.

As detailed in Section 6.1.1, change from baseline FST results in decibels for the two sites will be analyzed together. However, analysis of raw FST results in decibels will be separate for the two sites due to differences in the scale of absolute decibel values. Analysis of FST results in log units will also be separate for the two sites.

3.2. General Analysis Specifications

3.2.1. Global Analysis Principles

Unless otherwise specified, analyses will be descriptive and performed based on the safety population defined in Section 3.3.

The baseline for a given parameter is defined as the last assessment for this parameter before first administration of the investigational medicinal product (IMP), unless otherwise specified.

Continuous variables will be summarized using number of available data (N), mean, standard deviation (SD), median, minimum, and maximum for each cohort and overall. Collected continuous variables that will be summarized include:

- Age
- Height
- Weight
- Body mass index (BMI)
- Diastolic blood pressure (DBP)
- Systolic blood pressure (SBP)
- Heart rate (HR)
- Body temperature
- Hematology and Chemistry laboratory results
- BCVA
- FST
- Intraocular pressure (IOP)
- LLVA
- Photoaversion
- Pupillometry
- OCI
- NEI VFQ-25/CVAQC
- OCT measurements (EDC)
 - Total retinal thickness at the fovea
 - Thickness of perifovea five degrees superior/inferior/temporal/nasal
- OCT measurements (MERIT)
 - Mean retinal thickness
 - Outer nuclear layer (ONL) thickness at the fovea
 - Distance from inner segment (IS)/outer segment (OS)-inner boundaries of the retinal pigment epithelium (RPE) (outer segment measurement) at the fovea and in rod dominant region of the bleb
 - Distance from external limiting membrane (ELM)-IS/OS (inner segment measurement) at the fovea and in the rod dominant region of the bleb
 - Thickness of perifovea five degrees superior/inferior/temporal/nasal
 - Mean inner retina thickness at the fovea
 - Mean retinal thickness in the rod dominant region of the bleb
 - Ellipsoid zone (EZ) width within central 5 millimeters (mm) at the fovea

Categorical and ordinal data will be summarized using number and percentage of subjects in each cohort and overall. Denominators for percentages will be the number of subjects in each cohort and overall, in the safety population (defined in Section 3.3) with data at the respective visit, as appropriate. Collected variables that will be summarized categorically include:

- Gender
- Race
- Ethnicity
- Urinalysis laboratory results
- Humoral immune response
- Cellular immune response
- Slit lamp assessment findings
- Ophthalmoscopy findings
- Features in fundus photography
- PECV
- OCT features (EDC)
 - Assessment of an EZ line extending +/- 5 degree from fovea
 - Assessment of fovea bulge
- OCT features (MERIT)
 - Cystoid macular edema (CME) presence
 - Epiretinal membrane presence
 - Foveal distortion
 - Foveal EZ line
 - Normal retina/fovea contour
 - Retinal striae
 - Vitreous debris/cells

Time (e.g., duration) will be calculated as follows:

- For visits (or events) that occur on or after administration of IMP, time will be calculated as:

$$time (days) = visit (or event) date - IMP administration date + 1$$

- For visits (or events) that occur prior to administration of IMP, time in days will

$$time (days) = IMP administration date - visit (or event) date$$

- For listings (e.g., for AEs), the number of days since administration of IMP is defined as:

$$days since IMP administration = event date - IMP administration date + 1$$

3.2.2. Reporting Conventions

In general, all data will be listed, sorted by cohort, subject, and when appropriate by time point within subjects. All summary tables will present results by cohort as well as overall, as appropriate.

P-values will be reported to two decimal places. P-values less than 0.005 will be reported as “<0.01” and p-values greater than 0.995 and less than 1 will be reported as “>0.99”.

The mean, SD, and median will be reported to one decimal place greater than the original data. The minimum and maximum will use the same number of decimal places as the original data.

Percentages will be reported to the nearest whole number, unless otherwise specified. Values greater than zero and <0.5% will be presented as “<1”, and values greater than 99.5% and less than 100% will be reported as “>99”.

For all other estimators, the NEJM statistical reporting guidelines will be followed: results will be presented with no more precision than is of scientific value and is meaningful. Results derived from models will be limited to the appropriate number of significant digits.

3.2.3. Analysis Software and Other Technical Details

Statistical analyses will be performed using SAS v9.4 or higher or R v3.6.1 or higher. All tables, listings and figures presented in the analysis will be created using either SAS v9.4 or R v.3.6.1 or higher.

3.3. Analysis Populations

Screened Population: Includes all subjects who have signed informed consent.

Safety Population: Includes all Screened Population subjects who received study treatment.

3.3.1. Study Periods

This study is broken down into the following periods:

- The **screening period** includes all screening visits (Day -56 to Day -8).
- The **baseline period** includes all baseline visits (Day -7 to Day -1).
- The **treatment period** includes the visit of IMP administration (Day 1).
- The **main study follow-up period** includes all visits following IMP administration up to and including Week 52.
- The **extension study follow-up period** includes all visits from the end of the main study follow-up period (Week 52) to the end of study Week 260 visit.

For all safety data, the observation period will be divided into two segments:

- The **pre-treatment period** is defined as the time between informed consent signature and IMP administration.
- The **treatment-emergent adverse event (TEAE) period** is defined as the time from IMP administration through Week 260 or discontinuation of the study, whichever occurs earlier.

3.4. Handling of Missing Data

For the analysis of safety variables, only partial dates may be imputed; otherwise, missing data will be treated as missing.

The algorithm for imputing partial AE start and end dates is as follows:

- Start date:
 - If day is missing,
 - If the start month and year are the same as the month and year of IMP administration, then the day is imputed to the day of IMP administration or the day of the AE end date (possibly imputed), whichever is earlier.
 - If the start month and year are not the same as the month and year of IMP administration, then the day is imputed to the first of the month.
 - If month and day are missing,
 - If the start year is the same as the year of IMP administration, and the AE end date is available and is prior to IMP administration, then the day and month are imputed to the AE end date. Otherwise, the day and month are imputed to the month and day of IMP administration.
 - If the start year is not the same as the year of IMP administration, then the month and day are imputed to January 1.
- End date:
 - If day is missing, then the day is imputed to the last day of the month.
 - If month and day are missing, then the month and day are imputed to December 31.
 - If the imputed date is later than the date of death (if available), then the date of death will be used as the imputed date.

The algorithm for imputing all other partial start and end dates is as follows:

- Start date: If day is missing, then the day is imputed to the first of the month. If month and day are missing, then the month and day are imputed to January 1.
- End date: If day is missing, then day is imputed to the last day of the month. If month and day are missing, then the month and day are imputed to December 31.

4. SUMMARY OF STUDY CONDUCT AND SUBJECTS

4.1. Disposition of Subjects

The total number of subjects in each of the following populations as defined in Section 3.3 will be summarized using counts and percentages by cohort and overall ([Table 1](#)):

- Screened population
- Safety population

Reasons for discontinuation from the study will be presented within the safety population in [Table 1](#).

Subject flow as outlined in [Figure 1](#) will also be presented.

Subjects who withdrew from the study will be listed along with the reason for withdrawal ([Listing 1](#)). All withdrawals from the study, taking place on or after IMP/non-investigational medicinal product (NIMP) administration, will be fully documented in the body of the CSR.

4.2. Subject Demographic Characteristics, Medical History and Diagnoses

The following subject demographics collected at the Screening (Day -56 to Day -8) and/or Baseline (Day -7 to Day -1) visits will be summarized in the safety population by cohort and overall ([Table 2](#)):

- | | |
|-------------|----------|
| • Age | • Height |
| • Gender | • Weight |
| • Race | • BMI |
| • Ethnicity | |

Subject demographics will also be listed along with genetic testing results ([Listing 2](#)).

Medical history, collected at the Screening and/or Baseline visits, will be summarized in the safety population by cohort and overall, by system organ class (SOC) and preferred term (PT) ([Table 3](#)). Medical history will also be listed ([Listing 3](#)).

4.3. Extent of Study Treatment Exposure and Compliance

The extent of study therapy exposure (ATSN-101) and compliance will be assessed and summarized by cohort and overall, for subjects in the safety population ([Table 4](#)). The number and percentage of subjects receiving the full 300 µL dose along with a summary of the dose administered will be presented.

Treatment exposure and compliance will also be listed for subjects in the safety population ([Listing 4](#)).

4.4. Prior/Concomitant Medication/Therapy

Medications will be coded according to the World Health Organization Drug Dictionary (WHO Drug Dictionary, last available version before database lock). Medications will be summarized by Anatomical Therapeutic Chemical (ATC) 1 and 2 (ATC1 and ATC2) codes for each cohort and overall, within the safety population. Subjects will only be counted once if they take the same generic medication more than once.

Concomitant medications with the IMP will be summarized separately (**Table 5**). Prior and concomitant medications will be listed separately (**Listing 5** and **Listing 6**, respectively).

Additionally, NIMP usage will be listed for each subject in the safety population (**Listing 7**). Per the protocol, the NIMP regimen includes prednisone, triamcinolone acetonide, prednisolone, and trimethoprim and polymyxin B.

4.5. Protocol Deviations

During review of the database, compliance with the protocol will be examined with regard to inclusion and exclusion criteria, treatment compliance, prohibited therapies, and timing and availability of planned assessments. Protocol deviations will be identified by the study team before database lock and listed in the Data Review and Surveillance Report, including missing data and study drug discontinuations, and classified as major or minor deviations.

Protocol deviations will be summarized by deviation coded term and deviation category for each cohort and overall, for all enrolled subjects in the study (**Table 6**).

General categories of major deviations include:

- Subjects who deviated from any entry criterion
- Subjects who did not receive IMP

Any major deviations will be listed by subject and/or described in the body of the CSR (**Listing 8**). All protocol deviations will also be listed by subject (**Listing 9**).

5. ANALYSIS OF SAFETY DATA

5.1. Analysis of Primary Endpoint

The primary objective is to evaluate the safety and tolerability of ascending doses of ATSN-101 administered as a unilateral subretinal injection in subjects with LCA caused by autosomal recessive *GUCY2D* mutations.

The primary analyses will be based on the incidence of AEs in subjects in the safety population at 52 weeks. An additional safety analysis will be performed at Week 260, the end of the Extension Study Period. As part of the analyses, the number and percentage of subjects with AEs, SAEs, and AESIs will be summarized in each cohort and overall. Significant changes from baseline in other safety assessments will also be assessed.

Analyses of safety data will be based on the safety population.

5.1.1. Adverse Events

AEs will be coded to a “Preferred Term (PT)” and “High Level Group Term (HLGT)”, “High Level Term (HLT)” and primary “System Organ Class (SOC)” using the Medical Dictionary for Regulatory Activities (MedDRA, version currently in use by the Sponsor at the time of database lock). AE severity will be graded according to Common Terminology Criteria for Adverse Events (CTCAE, v5.0).

AEs will be classified into predefined standard categories according to chronological criteria:

- **Pre-treatment AEs:** AEs that occurred or worsened during the pre-treatment period.
- **Treatment-emergent AEs (TEAEs):** AEs that occurred or worsened during the TEAE period.

Pre-treatment AEs will not be summarized or listed.

TEAEs will be listed, sorted by subject, onset date and time ([Listing 10](#)).

5.1.1.1. Treatment-emergent Adverse Events

An overview of TEAEs for subjects in the safety population in each cohort and overall will include the number and percentage of subjects with any TEAE, any serious TEAE, any severe TEAE (CTCAE Grade 3 or above), any AESI, any TEAE leading to death (if any occurred), any TEAE leading to permanent treatment discontinuation, any related TEAE (to IMP, NIMP, study procedures, or surgical procedure), and no AEs ([Table 7](#)). [Table 7](#) will also summarize TEAEs severity and relatedness to IMP, NIMP, study procedures and surgical procedure, and outcome.

An additional table will show the number and percentage of subjects in each cohort and overall, with TEAEs and the number of occurrences of TEAEs in each cohort and overall broken down by SOC, PT, and severity ([Table 8](#)). TEAEs related to IMP, NIMP, study procedures, and surgical procedure will be summarized separately, as necessary ([Table 9](#) – [Table 12](#)).

5.1.1.2. Deaths and Serious Adverse Events

Any deaths and serious AEs will be listed ([Listing 11](#) and [Listing 12](#), respectively).

An overview of serious TEAEs, similar to that for TEAEs, will be generated for subjects in the safety population in each cohort and overall ([Table 13](#)).

An additional table will summarize serious TEAEs by SOC, PT, and severity in each cohort and overall ([Table 14](#)). Serious TEAEs related to surgical procedure will be summarized ([Table 15](#)).

5.1.1.3. Adverse Events Leading to Treatment Discontinuation

Any AEs leading to permanent treatment discontinuation will be listed ([Listing 13](#)).

5.1.1.4. Adverse Events of Special Interest

AESIs are defined in Section 11.3.2 of the protocol. The number and percentage of subjects experiencing a treatment emergent AESI will be presented by SOC and PT, sorted by decreasing incidence of PT within each SOC ([Table 16](#)). AESIs will also be listed ([Listing 14](#)).

5.1.2. Ophthalmological Safety Endpoints

Ocular examinations as part of the assessment of ophthalmological safety endpoints include:

- Slit lamp examination
- IOP
- Ophthalmoscopy
- Fundus photography

Changes in safety endpoints from baseline will be summarized at each visit for the treated and untreated eyes. In addition, where appropriate, individual profile plots and plots of mean change in the variable over time will be presented.

The primary endpoint will be considered the Week 52 visit.

5.1.2.1. Slit Lamp Examination

A slit lamp examination is performed at all visits, except Day 1, the day of the surgery. As part of the slit lamp examination, the eyelid, conjunctiva, cornea, iris/pupil, and anterior chamber are evaluated along with nuclear sclerosis, cortical changes, and posterior subcapsular changes in the lens for both the treated and untreated eyes. The eyelid, conjunctiva, cornea, and iris/pupil are assessed as normal, abnormal not clinically significant, and abnormal clinically significant. Anterior chamber flare levels are assessed as none, faint, moderate, marked, and intense. The lens nuclear sclerosis, cortical changes, and posterior subcapsular are assessed as none, mild, moderate, pronounced, and severe.

A shift table for anterior chamber flare assessment will summarize the change from baseline at follow-up visits by cohort and overall, for the treated and untreated eyes for subjects in the safety population ([Table 17](#)). Individual slit lamp examination results for all assessments will be listed ([Listing 15](#)).

5.1.2.2. Ophthalmoscopy

Ophthalmoscopy is performed at all visits, except Day 1. As part of the ophthalmoscopy assessment, the macula, optic disc, peripheral retina, choroid, and vitreous are evaluated for the treated and untreated eyes. The macula, optic disc, peripheral retina, and choroid are assessed as normal, abnormal not clinically significant, and abnormal clinically significant. The vitreous is assessed as clear, trace, few opacities, significant blurring, optic disc visibility, and optic disc not visible.

Shift tables for macular and vitreous assessments will summarize the change from baseline at follow-up visits by cohort and overall, for the treated and untreated eyes for subjects in the safety population ([Table 18](#) and [Table 19](#), respectively). Individual ophthalmoscopy results for all assessments will be listed ([Listing 15](#)).

5.1.2.3. Intraocular Pressure

IOP is assessed at all visits, except Day 1.

IOP values over time and change in IOP from baseline will be summarized by cohort and overall, for the treated and untreated eyes for subjects in the safety population ([Table 20](#) and [Table 21](#), respectively). Additionally, mean IOP and mean change in IOP from baseline will be plotted over time for the treated and untreated eyes by cohort ([Figure 2](#) and [Figure 3](#), respectively).

Individual IOP over time and change from baseline over time for each subject will be plotted by treated and untreated eye ([Figure 4](#) and [Figure 5](#), respectively). IOP values will also be listed ([Listing 16](#)).

5.1.2.4. Fundus Photography

Fundus photography is performed at the Screening, Baseline, Day 2, and Day 3 visits as well as all visits starting at Day 28 in both eyes to document fundus appearance. At follow-up visits, fundus appearance is assessed for a change from baseline as well as whether the change was clinically significant, if there was a change from baseline.

Individual fundus photography results will be listed ([Listing 17](#)).

5.1.3. Clinical Laboratory Evaluations

For hematology, chemistry, and urinalysis parameters with laboratory ranges and/or abnormality criteria (potentially clinically significant abnormalities [PCSAs] as listed in Appendix 1), analyses will be performed using all post-baseline assessments done during the TEAE period, including all unplanned and rechecked values. Values will be flagged when outside the laboratory limits and/or when reaching the PCSA criteria.

The number and percentage of subjects with post-baseline PCSAs according to baseline status will be presented by cohort and overall for subjects in the safety population ([Table 22](#)). A listing of individual data from subjects with post-baseline PCSAs will be provided ([Listing 18](#)).

The number and percentage of subjects with hematology and chemistry laboratory values out of normal range during the treatment-emergent period will also be summarized by cohort and overall for subjects in the safety population ([Table 23](#) and [Table 24](#), respectively) and listed ([Listing 19](#)).

Individual hematology, chemistry, and urinalysis results will be listed ([Listing 20](#), [Listing 21](#), and [Listing 22](#), respectively).

5.1.4. Immunogenicity

Measurements of antibodies to the AAV5 capsid and RetGC1 will be performed prior to and after vector administration as markers of the humoral immune response. Samples will also be taken for measurement of the cellular immune response to AAV5 and RetGC1 by ELISpot, though these will be frozen and only run if there is evidence of ocular inflammation.

Assay Positivity (ADA and ELISpot)

The number and percentage of subjects with positive anti-drug antibodies (ADA) (AAV5 and RetGC1) and detected ELISpot results (AAV5 and RetGC1) will be presented by cohort and by visit (**Table 25 – Table 27**). Individual ADA and ELISpot results will also be listed (**Listing 23 – Listing 25**).

Additionally, individual anti-AAV5 and anti-RetGC1 titer results will be plotted over time by cohort (**Figure 6** and **Figure 7**, respectively).

Treatment-Emergent Positivity (ADA and ELISpot)

The number and percentage of subjects with treatment-emergent positive ADA (AAV5 and RetGC1) and ELISpot results (AAV5 and RetGC1) will be presented by cohort and by visit (**Table 28** and **Table 29**). Treatment-emergent positive ADA and ELISpot results will also be listed (**Listing 26 – Listing 29**).

Treatment-emergent positive result for ADA is defined as the following:

- A post-baseline result that is positive when the baseline result is negative.
- A post-baseline result that has a titer greater than or equal to 4 times the baseline titer when the baseline result is positive, while titer values are available at both baseline and post-baseline visits. It has previously been reported that a difference in titer values of at least twice the dilution level is considered to be significant; therefore, since a twofold serial dilution is performed in the ADA assay, a fourfold difference in titer values was selected as the threshold for significant change [1].

Treatment-emergent positive result for ELISpot is defined as the following:

- The treatment-emergent positive for each analyte (AAV5 and RetGC1) is defined as a post-baseline result that has a fold increase ≥ 2 relative to baseline. The % coefficient of variation (CV) for each triplicate is required to be ≤ 25 -50% depending on the mean spot count, and a two-fold (200%) increase relative to baseline was conservatively selected to be approximately 3x the CV (150%).

Relationship Between Immunogenicity Assay and Safety

The relationship between the immunogenicity assays (ADA and ELISpot) and selected adverse events will be assessed. These adverse events include AESIs and SAEs. The number and percentage of AESIs and SAEs will be summarized by (1) subjects with positive/negative (ADA) assay at baseline and subjects with detected/not detected/no result (ELISpot) assay at baseline (**Table 30 – Table 33**); and (2) subjects with at least one treatment-emergent positive assay at any visit during the study and subjects with no treatment-emergent positive assay during the study (**Table 34 – Table 37**). For ELISpot, the relationship with the selected adverse events will be summarized with respect to either AAV5 or RetGC1. AESIs and SAEs for subjects with positive ADA assays at baseline and detected ELISpot assays at baseline will be listed (**Listing 30 – Listing 33**). Similarly, AESIs and SAEs for subjects with at least one treatment-emergent positive immunogenicity assay will be listed (**Listing 34 – Listing 37**).

5.1.5. Vital Signs

For all vital signs assessed, the values to be used as baselines will be the Day 1 pre-dose assessment values.

HR, SBP, and DBP at each visit and change from baseline will be summarized using descriptive statistics (including mean, SD, median, minimum and maximum) by cohort and overall (**Table 38 – Table 40**), respectively). Mean HR, SBP, and DBP will also be plotted over time by cohort (**Figure 8 – Figure 10**, respectively).

Individual vital sign results will be listed (**Listing 38**).

For all parameters, the number and percentage of subjects with PCSAs (listed in Appendix 1) will be summarized by cohort and overall, for subjects in the safety population, regardless of baseline status (**Table 41**). A listing of individual data from subjects with post-baseline PCSAs will be provided (**Listing 39**). A listing of vital signs outside of normal range will also be provided (**Listing 40**). Abnormal baseline vital signs will be defined as those meeting the PCSA criteria listed in Appendix 1. Any change from baseline will not be considered for abnormality assessment at baseline.

5.2. Additional Safety Analysis

5.2.1. Adverse Events (AEs)

An additional safety analysis will be performed at Week 260, the end for the Extension Study Period. The number and percentage of subjects in the safety population in each cohort and overall with AEs and the number of occurrences of AEs in each cohort and overall will be tabulated by length of follow-up (Weeks 0-52, 53-104, 105-156, 157-208, and 209-260 as well as Weeks 0-260) (**Table 42**). SAEs and AESIs will also be summarized similarly (**Table 43** and **Table 44**, respectively).

6. ANALYSIS OF EFFICACY DATA

6.1. Analysis of Secondary Efficacy Endpoints

The secondary objective is to evaluate the efficacy of ascending doses of ATSN-101 administered as a unilateral injection in subjects with *GUCY2D*-LCA.

The secondary efficacy endpoints include:

- FST – FST is performed at all visits in both treated and untreated eyes, except Day 1, Day 2, and Days 4-7. For Days 8, 9, 10, 12, and 14, FST will be performed on one or more of the five visits based on the Investigator's judgement. FST is performed in both light- and dark-adapted states for three stimulus colors – red, white, and blue.
- BCVA – BCVA is assessed at all visits in both treated and untreated eyes, except Day 1. BCVA will be expressed both as LogMAR and as Early Treatment Diabetic Retinopathy Study (ETDRS) letters (when available). For subjects unable to identify the largest line of letters on the ETDRS chart, off chart BCVA measurements will be collected (counting fingers, hand motion perception, light perception, no light perception) and will be assigned a LogMAR value. Hand motion will be assigned a LogMAR of 3.0 and light perception will be assigned a LogMAR of 4.0. In addition, the Berkeley Rudimentary Vision Test (BRVT) will also be applied for subjects with off chart BCVA.

Efficacy endpoints will be summarized with descriptive statistics at each visit, for each cohort and overall, with the main analysis occurring at 52 weeks. An additional analysis will be performed at Week 260. These analyses will be performed for treated and untreated eyes separately.

Descriptive statistics (mean, SD, median, minimum, and maximum for continuous variables; count and percentages for categorical variables) will be provided by cohort and overall for all efficacy-related parameters. The difference between baseline and post-operative values in both treated and untreated eyes and the difference between treated and untreated eyes will be summarized similarly.

The difference between the treated and untreated eyes for a given subject will be calculated as the treated eye result minus the untreated eye result, and the difference between baseline and post-operative visit will be calculated as post-operative visit minus the baseline.

For each cohort, statistical analyses for secondary efficacy measures (e.g., FST and BCVA) will be performed for comparing their changes from baseline between treated eyes vs. untreated control eyes using paired t-test for each follow-up time point separately (Day 28 and after). The following hypothesis will be tested:

$$H_0: \Delta_{Treated\ eye} = \Delta_{Untreated\ eye}$$

versus the alternative

$$H_1: \Delta_{Treated\ eye} \neq \Delta_{Untreated\ eye}$$

Where $\Delta_{Treated\ eye}$ and $\Delta_{Untreated\ eye}$ represent the mean change from baseline for the treated and untreated eyes, respectively. In SAS, the paired t-tests will be carried out for comparing treated eye vs. untreated eye at each follow-up time point using PROC TTEST.

For comparing the overall differences between treated eyes and untreated eyes in their changes from baseline during the whole follow-up period, longitudinal analyses of all data from follow-up times combined (Day 28 and after) will be performed, and generalized estimating equations (GEE) with independent working correlation structure will be used to account for repeated measures correlation for inter-eye difference over time. In SAS, the GEE model will be carried out using PROC GENMOD using a repeated statement for subject.

The same analyses for comparison of changes from baseline between the treated and untreated eyes will also be carried out for the high-dose cohorts (Cohorts 3, 4, and 5) together. All analyses will be carried out at a significance level of 0.05.

In addition, where appropriate, individual profile plots and mean plots of changes in the measures against time by cohort will be presented. These plots will be produced for the treated and untreated eye.

Efficacy analyses will be performed based on subjects in the safety population who have both the baseline and at least one post-baseline examination for the specific endpoint measurement that will be included in the analysis.

6.1.1. Full-field Stimulus Testing

Multiple FST measurements are taken at visits for each eye, state, and stimulus color, and sensitivities are recorded in the clinical database in decibels (dB). The average of the FST measurements for each visit, eye, state, and stimulus color will be used in all presentations and analyses.

6.1.1.1. Decibels

Summaries for raw FST dB values will be presented separately between the two sites due to differences in the scale of absolute dB values. However, change from baseline FST dB values will be analyzed together for the two sites.

Additionally, for analyses in dB, FST values for the OHSU site will be multiplied by -1, so that increasing dB will indicate improvement in FST for both sites. Due to the small number of subjects enrolled at the OHSU site, raw individual FST dB values will only be plotted and listed.

FST change from baseline values (both sites together) will be summarized by cohort, state, and stimulus color for both the treated and untreated eyes ([Table 45](#) – [Table 50](#)). Additionally, mean FST dB values (UPenn) and mean change in FST from baseline (both sites together) will be plotted over time for the treated and untreated eyes by cohort, state, and stimulus color ([Figure 11](#) and [Figure 12](#), respectively).

Additionally, the difference between the treated and untreated eyes' FST change from baseline values (both sites together) will be similarly summarized ([Table 51](#) – [Table 56](#)) by cohort, state, and stimulus color.

Furthermore, as described in Section 6.1, analysis comparing the change from baseline between the treated and untreated eyes will be carried out. Results for each cohort, visit (Day 28 and after), and stimulus color will be presented in [Table 57](#) and [Table 58](#), respectively, for the dark and light adapted states. The same analysis will be carried out for the high-dose cohorts (Cohorts 3, 4, and 5). Results for the analysis including the high-dose cohorts (Cohorts 3, 4, and 5) will also be presented in [Table 57](#) and [Table 58](#), respectively, for the dark and light adapted states. The following additional figures will also be generated: 1) A plot of the mean change ($\pm$ standard error [SE]) in dark adapted FST values in dB over time (excluding visits between baseline and Day 28) for the high-dose cohorts by eye and stimulus color ([Figure 13](#)), and 2) A plot of the mean change ($\pm$ SE) in treated eye dark adapted FST values in dB over time (excluding visits between baseline and Day 28) for Cohort 1, Cohort 2, and the high-dose cohorts by stimulus color ([Figure 14](#)).

Individual FST values over time in dB and change from baseline over time for each subject will be plotted by eye (treated eye, untreated eye), state, and stimulus color ([Figure 15](#) – [Figure 17](#)). Additionally, spaghetti plots for individual FST values in dB (UPenn) and change from baseline (both sites together) by eye, state, and stimulus color will be generated ([Figure 18](#) and [Figure 19](#)). FST values in dB will also be listed for both sites ([Listing 41](#) and [Listing 42](#)).

6.1.1.2. Log Units

For FST in log units, separate analyses will be performed for the two sites due to the use of different testing protocols at each site.

Sensitivities in dB for each site will be converted to log units using the following formulas [2]:

UPenn:

$$\log_{10}(L) = \log_{10}(L_{0,FST2}) - S/10$$

Where L is the calculated luminance in cd/m^2 , $L_{0,FST2}$ is the reference luminance equal to $3.7 \text{ cd}/\text{m}^2$ and S is the sensitivity in dB.

OHSU:

$$\log_{10}(L) = \log_{10}(L_{0,D-FST}) + S/10$$

Where L is the calculated luminance in $\text{cd.s}/\text{m}^2$, $L_{0,D-FST}$ is the reference luminance equal to $1.0 \text{ cd.s}/\text{m}^2$ and S is the sensitivity in dB.

FST values and change from baseline in log units will be listed by eye, state and stimulus color for both sites ([Listing 43](#) and [Listing 44](#)).

6.1.2. Best-Corrected Visual Acuity

BCVA results in logMAR and ETDRS letters and their change in BCVA from baseline will be summarized by cohort for the treated and untreated eyes (

[Table 59](#) – [Table 62](#)). Additionally, mean BCVA in logMAR and ETDRS letters and mean change in BCVA from baseline will be plotted over time for the treated and untreated eyes by cohort ([Figure 20](#) – [Figure 23](#)).

The difference in BCVA in logMAR and ETDRS letters between the treated and untreated eyes and change from baseline will be similarly summarized by cohort ([Table 63](#) and [Table 64](#)).

Furthermore, as described in Section 6.1, analysis comparing the change from baseline between the treated and untreated eyes will be carried out for both logMAR and ETDRS letters. Results for each cohort (for each visit and overall) will be presented in [Table 65](#) and [Table 66](#), respectively, for logMAR and ETDRS letters. Results for the analysis including only the high-dose cohorts will also be presented in [Table 65](#) and [Table 66](#), respectively, for logMAR and ETDRS letters. The following additional figure will also be generated: A plot of the mean change ($\pm$ SE) in BCVA values in logMAR over time (excluding visits between baseline and Day 28) for Cohort 1, Cohort 2, and the high-dose cohorts by eye ([Figure 24](#)).

Individual BCVA values over time in logMAR and ETDRS letters and change from baseline over time for each subject will be plotted by eye ([Figure 25](#) – [Figure 28](#)). Additionally, spaghetti plots for individual BCVA values in logMAR and change from baseline by eye will be generated ([Figure 29](#) and [Figure 30](#), respectively). BCVA values in logMAR and ETDRS letters will also be listed ([Listing 45](#) and [Listing 46](#), respectively).

6.2. Analysis of Exploratory Endpoints

Analysis of exploratory efficacy parameters, including pupillometry, OCI, photoaversion, LLVA, OCT, visual function questionnaire, PECV, and mobility testing, will be similar to what is described in Section 6.1, with the exception of the p-value testing and summaries of the difference between the treated and untreated eyes

Analysis of exploratory endpoints will be performed based on subjects in the safety population who have both the baseline and at least one post-baseline examination for the specific endpoint measurement that will be included in the analysis.

6.2.1. Pupillometry

Pupillometry is performed at the Screening and Baseline visits as well as at all post-treatment visits starting at Day 28 through Week 52 (protocol amendment 08, effective 13 September 2023). Prior to protocol amendment 08, pupillometry was performed at the Screening and Baseline visits as well as at all post-treatment visits starting at Day 28. Testing may also be performed at additional visits based on Investigator judgement.

Separate analyses will be carried out for the two sites as different pupillometry data is collected for UPenn and OHSU subjects.

6.2.1.1. University of Pennsylvania Site

All pupillometry values collected for UPenn subjects will be listed ([Listing 47](#)).

6.2.1.1.1. Transient Pupillary Light Reflex Amplitude

Transient pupillary light reflex (TPLR) amplitude is defined as the difference between the pupil diameter at a fixed time (0.9 seconds [s]) after the onset of the light stimulus and the pre-stimulus baseline values. At visits, TPLR amplitude at 0.9s is reported for both eyes at seven different light intensities (log luminance (cd/m^2): -3.3, -2.3, -1.3, -0.3, 0.7, 1.7, and 2.7) for two light stimulus colors (red and blue).

TPLR amplitudes and change from baseline by eye, stimulus color and intensity will be listed ([Listing 48](#)).

6.2.1.1.2. Transient Pupillary Light Reflex Response Threshold

The TPLR response threshold is defined as the threshold stimulus intensity evoking an amplitude of 0.3 mm [3]. The threshold stimulus intensity evoking an amplitude of 0.3mm will be determined by modelling the amplitude at 0.9s versus the light intensity for each visit, stimulus color, and eye for a subject using the following nonlinear sigmoid model:

$$\text{Amplitude at 0.9s} = \frac{a}{\left(1 + \exp\left(\frac{b - \text{intensity}}{c}\right)\right)}$$

The data will be modelled in R using the nls function in the stats package. Starting values for a, b, and c will be estimated using the SSlogic function in the stats package. The TPLR response thresholds at an amplitude of 0.3mm will then be calculated by using the coefficients from the nonlinear model and solving for the intensity when the amplitude at 0.9s is 0.3mm:

$$\text{intensity} = b - c \times \log\left(\frac{a}{0.3} - 1\right)$$

Response thresholds cannot be calculated when all amplitudes for a certain subject, eye, visit, and stimulus color are less than 0.3mm or when the nonlinear model fails to converge. Response thresholds that cannot be calculated will be treated as missing.

Change in TPLR response threshold from baseline will be summarized by cohort and stimulus color for the treated and untreated eyes (Table 67 and Table 68, respectively). Additionally, mean TPLR response threshold and mean change in TPLR response from baseline will be plotted over time for the treated and untreated eyes by cohort and stimulus color (Figure 31 and Figure 32, respectively).

TPLR response thresholds will also be listed by eye and stimulus color (Listing 49).

6.2.1.2. Oregon Health and Science University Site

For OHSU subjects, pupillometry data collected include:

- Pre-stimulus diameter – the maximum pupil size before constriction (mm)
- Minimum diameter – pupil diameter at peak constriction (mm)
- Latency – time of onset of constriction following initiation of light stimulus (milliseconds [ms])
- 75% recovery – time to reach 75% of the original baseline pupil diameter after the peak of the constriction (ms)
- Percent change – percentage of change from baseline diameter to peak constriction (%)
- Constriction velocity – average velocity of pupil constriction (mm/s)
- Maximum constriction velocity – maximum velocity of pupil constriction (mm/s)
- Dilation velocity – average velocity of recovery/dilation to initial resting size after reaching peak constriction (mm/s)

Three values for each of the above measurements are provided at all visits for both eyes. The average of the values will be used in all presentations.

Pupillometry results will be listed ([Listing 50](#)).

6.2.2. Oculomotor Instability

Oculomotor instability is performed at the Screening and Baseline visits as well as at all post-treatment visits starting at Day 28 through Week 52 (protocol amendment 08, effective 13 September 2023). Prior to protocol amendment 08, oculomotor instability was performed at the Screening and Baseline visits as well as at all post-treatment visits starting at Day 28. Testing may also be performed at additional visits based on Investigator judgement. Both mean gaze offset and oculomotor instability are measured at visits with internal fixation turned either on or off. An overall OCI measurement will also be calculated, for internal fixation turned off and on, as the sum of the mean gaze offset and oculomotor instability results for the respective fixation. The overall OCI measurement is provided from MERIT but will be calculated for data from EDC.

Change in overall OCI measurement from baseline will be summarized by cohort and fixation for the treated and untreated eyes ([Table 69](#) and [Table 70](#)). Mean gaze offset, oculomotor instability, and overall OCI measurement will be listed by eye and fixation ([Listing 51](#)).

6.2.3. Photoaversion

Photoaversion is assessed at the Baseline visit as well as at all post-treatment visits starting at Day 28 through Week 52 (protocol amendment 08, effective 13 September 2023). Prior to protocol amendment 08, photoaversion was performed at the Baseline visit as well as at all post-treatment visits starting at Day 28. Testing may also be performed at additional visits based on Investigator judgement. A photoaversion threshold is determined by testing a series of increasing light intensities without dilation or dark adaptation and will be expressed as a measure of light intensity. Three values are provided at visits for both eyes. The average of the values will be used in all presentations and analyses.

Change in photoaversion threshold from baseline will be summarized by cohort for the treated and untreated eyes ([Table 71](#)).

Photoaversion thresholds will also be listed by eye ([Listing 52](#)).

6.2.4. Low-luminance Visual Acuity

LLVA is assessed at the Baseline visit as well as at all post-treatment visits starting at Day 28 through Week 52 (protocol amendment 08, effective 13 September 2023). Prior to protocol amendment 08, LLVA was performed at the Baseline visit as well as at all post-treatment visits starting at Day 28. Testing may also be performed at additional visits based on Investigator judgement. LLVA will be expressed as the number of ETDRS letters read correctly by the subject.

LLVA data will not be analyzed for the UPenn site due to measurement discrepancies.

Due to the small number of subjects enrolled at the OHSU site, only individual LLVA values will be listed.

LLVA values will be listed by eye ([Listing 53](#)).

6.2.5. Optical Coherence Tomography

OCT measurement is performed at the Screening and Baseline visits as well as at all post-treatment visits starting at Day 28. Testing may also be performed at additional visits based on Investigator judgement.

6.2.5.1. EDC Data

Change from baseline for retinal thickness at the fovea ([Table 72](#)) and EZ line extending +/- 5 degree from fovea ([Table 73](#)) will be summarized by cohort for the treated and untreated eyes.

Additionally, mean values for retinal thickness at the fovea and changes from baseline will be plotted over time for the treated and untreated eyes ([Figure 33](#) and [Figure 34](#)).

OCT measures will also be listed for each spectral domain OCT (SD-OCT) parameter ([Listing 54](#)).

6.2.5.2. MERIT Data

MERIT OCT data includes results from SD-OCT that are centered at the fovea and centered at the bleb. The OCT results will be analyzed as follows.

OCT Centered at the Fovea:

Change from baseline for the following OCT fovea parameters received from MERIT will be summarized by cohort for the treated and untreated eyes. Data from horizontal and verticals scans will be summarized separately.

- EZ line width within central 5mm – horizontal and vertical scans ([Table 74](#) and [Table 75](#))
- Mean retinal thickness – horizontal and vertical scans ([Table 76](#) and [Table 77](#))

Qualitative assessment of the foveal EZ line ([Table 78](#)) Mean changes from baseline for EZ line width within central 5mm and mean retinal thickness will also be plotted over time for the treated and untreated eyes ([Figure 35](#) and [Figure 36](#)).

OCT fovea values will also be listed for all parameters ([Listing 55](#)).

OCT Centered at the Bleb:

Change from baseline for OCT bleb mean retinal thickness ([Table 79](#)) received from MERIT will be summarized by cohort for the treated and untreated eyes.

Mean values from OCT bleb mean retinal thickness will be plotted over time for the treated and untreated eye ([Figure 37](#)).

OCT bleb values will also be listed for all parameters ([Listing 56](#)).

6.2.6. Visual Function Questionnaire

Visual function questionnaires will be completed by subjects at the Baseline, Day 28, Week 12, and Week 24 visits as well as at all visits starting at Week 52. For Cohorts 1-4, the NEI VFQ-25 will be used, and for Cohort 5, the 25-item CVAQC, which was developed and validated for use in children and young people with visual impairment, will be used. The questionnaires are administered in an interview format.

The NEI VFQ-25 will be scored according to the NEI VFQ-25 scoring algorithm in the user's manual. If the optional questions are answered (i.e., VFQ-39), the optional questions will be scored per the user's manual.

The CVAQC scores used in analyses will be determined by using a Rasch conversion calculator which will convert raw CVAQC scores into logarithmic scores [4]. Scores can range from -3.00 (higher visual ability) to +2.80 (lower visual ability).

Change in NEI VFQ-25 overall and subscale scores from baseline will be summarized by cohort (for Cohorts 1-4) ([Table 80](#)). Additionally, mean change in NEI VFQ-25 overall score from baseline will be plotted over time ([Figure 38](#)).

Change in CVAQC overall and subscale scores from baseline will similarly be summarized for Cohort 5 ([Table 81](#)). Mean change in CVAQC overall score from baseline will also be plotted over time ([Figure 39](#)).

NEI VFQ-25 and CVAQC individual question responses will be listed ([Listing 57](#) and [Listing 58](#)).

6.2.7. Patient's Experience Due to Changes in Vision Questionnaire

Subjects will complete the PECV questionnaire at the Day 28, Week 12, and Week 24 visits as well as at all visits starting at Week 52. The PECV questionnaire asks whether subjects have had any changes in vision since receiving IMP.

PECV results will be summarized by cohort and overall ([Table 82](#)). Individual PECV responses will also be listed ([Listing 59](#)).

6.2.8. Mobility Testing

Mobility testing will be used to determine if therapy improves the ability for subjects to navigate a controlled course at controlled light levels from baseline. Each site will pilot a different course. The OHSU site will use the course(s) developed by Ora, while the UPenn site will use the course developed by Spark. Where available, mobility testing will be completed for each eye at the Baseline, Day 28, Week 12, and Week 24 visits as well as at all visits starting at Week 52. Testing may also be performed at additional visits. Mobility testing scores will be determined by reading centers specific to each of the two sites. As such, results will be analyzed separately for the two sites.

Mobility testing results from Ora will not be provided to the Coordinating Center for analysis. Therefore, mobility testing will not be analyzed for the OHSU site.

For the UPenn site, the lowest light level at which the subject is able to pass will be mapped to the following multi-luminance mobility test (MLMT) score code, which will be used in analyses:

Luminance Level (Lux)	1	4	10	50	125	250	400	>400
MLMT Score Code	6	5	4	3	2	1	0	-1

The MLMT score code and change from baseline will be plotted over time for each subject for the UPenn site ([Figure 40](#) and [Figure 41](#)). Individual results will also be listed ([Listing 60](#)).

7. INTERIM ANALYSES

Interim analyses of safety and efficacy data will be performed after completion of the Week 52 follow-up visit of the last enrolled subject. Interim analyses may also be performed in case of unexpected safety concerns and/or for internal decision making.

8. SUMMARY OF CHANGES TO THE CONDUCT OF THE STUDY AND PLANNED ANALYSES

Changes to the analyses described in this statistical analysis plan will be fully documented in a revised version of the plan prior to locking the study database and conducting the primary outcome analysis at Week 52. Changes made after locking the study database will be described in the CSR. Similarly, any change to the analyses described herein that occur between Week 52 and Week 260 will be fully documented in a revised SAP. Changes made after locking the database at Week 260 will be described in the CSR.

9. QUALITY ASSURANCE

During the course of the study, the Sponsor or designee will make routine site visits to review protocol compliance to ensure the study is being conducted according to the relevant regulatory requirements.

The review of each subject's medical records will be performed in a manner that adequately maintains the subject's confidentiality.

Regulatory authorities may carry out on-site inspections or audits that may include source data checks. Therefore, direct access to the original source data will be required for inspections, audits, or both. All inspections and audits will be carried out with consideration of data protection as well as subject confidentiality.

10. REFERENCES

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APPENDICES

APPENDIX 1. POTENTIALLY CLINICALLY SIGNIFICANT ABNORMALITIES CRITERIA

Parameter	PCSA Criteria
Chemistry	
Albumin	≤ 25 g/L
Alkaline Phosphate	> 1.5 ULN
Alanine Aminotransferase	> 3 ULN
Aspartate Aminotransferase	> 3 ULN
Total Bilirubin	> 1.5 ULN
Urea Nitrogen	≥ 17 mmol/L
Cholesterol	≥ 7.74 mmol/L
Creatine Kinase	> 3 ULN
Chloride	< 80 mmol/L > 115 mmol/L
Creatinine	≥ 150 umol/L (Adults) $\geq 30\%$ change from baseline
Glucose	≤ 3.9 mmol/L and $< \text{LLN}$ ≥ 11.1 mmol/L (unfasted); ≥ 7 mmol/L (fasted)
Potassium	< 3 mmol/L ≥ 5.5 mmol/L
Sodium	≤ 129 mmol/L ≥ 160 mmol/L
Triglycerides	≥ 4.6 mmol/L
Hematology	
Basophils	$> 0.1 * 10^9/\text{L}$
Eosinophils	$> 0.5 * 10^9/\text{L}$ or $> \text{ULN}$ (if $\text{ULN} \geq 0.5 * 10^9/\text{L}$)
Hematocrit	≤ 0.37 v/v (Male); ≤ 0.32 v/v (Female) ≥ 0.55 v/v (Male); ≥ 0.5 v/v (Female)
Hemoglobin	≤ 115 g/L (Male); ≤ 95 g/L (Female) ≥ 185 g/L (Male); ≥ 165 g/L (Female) Decrease from baseline ≥ 20 g/L

Lymphocytes	$> 4 * 10^9/L$
Monocytes	$> 0.7 * 10^9/L$
Neutrophils	$< 1.5 * 10^9/L$ (Non-Black); $< 1 * 10^9/L$ (Black)
Platelet Count	$< 100 * 10^9/L$ $\geq 700 * 10^9/L$
Erythrocyte Count	$\geq 6 * 10^{12}/L$
Leukocyte Count	$< 3 * 10^9/L$ (Non-Black); $< 2 * 10^9/L$ (Black) $\geq 16 * 10^9/L$
Vital Signs	
Systolic Blood Pressure	≤ 90 mmHg and decrease from baseline ≥ 20 mmHg ≥ 180 mmHg and increase from baseline ≥ 20 mmHg
Diastolic Blood Pressure	≤ 50 mmHg and decrease from baseline ≥ 15 mmHg ≥ 105 mmHg and increase from baseline ≥ 15 mmHg
Heart Rate	≤ 50 beats/min and decrease from baseline ≥ 20 beats/min ≥ 120 beats/min and increase from baseline ≥ 20 beats/min

APPENDIX 2. TABLES

List of Tables

Table 1. Subject Disposition by Cohort.....	35
Table 2. Summary of Demographics by Cohort	36
Table 3. Summary of Medical History by Cohort	38
Table 4. Summary of Treatment Exposure and Compliance by Cohort.....	39
Table 5. Summary of Concomitant Medications by WHO Drug Classification and Cohort	40
Table 6. Summary of Protocol Deviations by Cohort.....	41
Table 7. Overview of TEAEs by Cohort	42
Table 8. Summary of TEAEs by System Organ Class, Preferred Term, Severity, and Cohort	44
Table 9. Summary of TEAEs Related to IMP by System Organ Class, Preferred Term, Severity, and Cohort	45
Table 10. Summary of TEAEs Related to NIMP by System Organ Class, Preferred Term, Severity, and Cohort	45
Table 11. Summary of TEAEs Related to Study Procedures by System Organ Class, Preferred Term, Severity, and Cohort.....	45
Table 12. Summary of TEAEs Related to Surgical Procedure by System Organ Class, Preferred Term, Severity, and Cohort.....	45
Table 13. Overview of Serious TEAEs by Cohort	45
Table 14. Summary of Serious TEAEs by System Organ Class, Preferred Term, Severity, and Cohort	45
Table 15. Summary of Serious TEAEs Related to Surgical Procedure by System Organ Class, Preferred Term, Severity, and Cohort.....	45
Table 16. Summary of AESIs by System Organ Class, Preferred Term, and Cohort	46
Table 17. Summary of Slit Lamp Assessments Over Time by Cohort - Anterior Chamber	47
Table 18. Summary of Ophthalmoscopy Assessments Over Time by Cohort – Macula	48
Table 19. Summary of Ophthalmoscopy Assessments Over Time by Cohort – Vitreous	49
Table 20. Summary of IOP (mmHg) Over Time by Cohort.....	51
Table 21. Summary of Changes in IOP (mmHg) from Baseline Over Time by Cohort	51
Table 22. Summary of Subjects with Post-baseline PCSAs in Laboratory Parameters by Cohort	52
Table 23. Summary of Subjects with Post-Treatment Hematology Laboratory Parameters Outside of Normal Range by Cohort.....	54

Table 24. Summary of Subjects with Post-Treatment Chemistry Parameters Outside of Normal Range by Cohort.....	56
Table 25. Summary of ADA AAV5 and RetGC1 Results Over Time by Cohort.....	58
Table 26. Summary of ELISpot to AAV5 Results Over Time by Cohort.....	59
Table 27. Summary of ELISpot to RetGC1 Results Over Time by Cohort	59
Table 28. Summary of Treatment-Emergent ADA Positivity Over Time by Cohort.....	60
Table 29. Summary of Treatment-Emergent ELISpot Positivity Over Time by Cohort.....	61
Table 30. Summary of AESIs by Baseline ADA Assay Result.....	62
Table 31. Summary of SAEs by Baseline ADA Assay Result	62
Table 32. Summary of AESIs by Baseline ELISpot Assay Result.....	63
Table 33. Summary of SAEs by Baseline ELISpot Assay Result	63
Table 34. Summary of AESIs by Treatment-emergent ADA Assay	64
Table 35. Summary of SAEs by Treatment-emergent ADA Assay	64
Table 36. Summary of AESIs by Treatment-emergent ELISpot Assay	64
Table 37. Summary of SAEs by Treatment-emergent ELISpot Assay	64
Table 38. Summary of Heart Rate Over Time by Cohort.....	65
Table 39. Summary of Systolic Blood Pressure Over Time by Cohort.....	65
Table 40. Summary of Diastolic Blood Pressure Over Time by Cohort	65
Table 41. Summary of Subjects with PCSAs in Vital Signs by Cohort	65
Table 42. Summary of Adverse Events by Follow-up Period and Cohort	66
Table 43. Summary of Serious Adverse Events by Follow-up Period and Cohort	66
Table 44. Summary of AESIs by Follow-up Period and Cohort	66
Table 45. Summary of Changes in FST (decibels) Over Time by Cohort– Red, Light Adapted (All Sites)	67
Table 46. Summary of Changes in FST (decibels) Over Time by Cohort– Red, Dark Adapted (All Sites)	67
Table 47. Summary of Changes in FST (decibels) Over Time by Cohort– White, Light Adapted (All Sites)	67
Table 48. Summary of Changes in FST (decibels) Over Time by Cohort– White, Dark Adapted (All Sites)	67
Table 49. Summary of Changes in FST (decibels) Over Time by Cohort– Blue, Light Adapted (All Sites)	68

Table 50. Summary of Changes in FST (decibels) Over Time by Cohort– Blue, Dark Adapted (All Sites)	68
Table 51. Summary of Difference in Change from Baseline in FST (decibels) Between the Treated and Untreated Eyes Over Time by Cohort – Red, Light Adapted (All Sites)	69
Table 52. Summary of Difference in Change from Baseline FST (decibels) Between the Treated and Untreated Eyes Over Time by Cohort – Red, Dark Adapted (All Sites)	69
Table 53. Summary of Difference in Change from Baseline FST (decibels) Between the Treated and Untreated Eyes Over Time by Cohort – White, Light Adapted (All Sites)	70
Table 54. Summary of Difference in Change from Baseline FST (decibels) Between the Treated and Untreated Eyes Over Time by Cohort – White, Dark Adapted (All Sites)	70
Table 55. Summary of Difference in Change from Baseline FST (decibels) Between the Treated and Untreated Eyes Over Time by Cohort – Blue, Light Adapted (All Sites)	70
Table 56. Summary of Difference in Change from Baseline FST (decibels) Between the Treated and Untreated Eyes Over Time by Cohort – Blue, Dark Adapted (All Sites)	70
Table 57. FST (decibels) Analysis Results – Dark Adapted	71
Table 58. FST (decibels) Analysis Results – Light Adapted.....	72
Table 59. Summary of BCVA (logMAR) Over Time by Cohort.....	72
Table 60. Summary of BCVA (ETDRS letters) Over Time by Cohort.....	72
Table 61. Summary of Changes in BCVA (logMAR) from Baseline Over Time by Cohort.....	72
Table 62. Summary of Changes in BCVA (ETDRS letters) from Baseline Over Time by Cohort	72
Table 63. Summary of Difference in BCVA (logMAR) Between the Treated and Untreated Eyes Over Time by Cohort	72
Table 64. Summary of Difference in BCVA (ETDRS letters) Between the Treated and Untreated Eyes Over Time by Cohort	72
Table 65. BCVA (logMAR) Analysis Results.....	73
Table 66. BCVA (ETDRS letters) Analysis Results	73
Table 67. Summary of Changes in TPLR Response Threshold from Baseline Over Time by Cohort – Red (UPenn)	73
Table 68. Summary of Changes in TPLR Response Threshold from Baseline Over Time by Cohort – Blue (UPenn)	73

Table 69. Summary of Changes in Overall OCI from Baseline Over Time by Cohort – Fixation Off	73
Table 70. Summary of Changes in Overall OCI from Baseline Over Time by Cohort – Fixation On	73
Table 71. Summary of Changes in Photoaversion Threshold Over Time by Cohort	73
Table 72. Summary of Changes in Retinal Thickness at the Fovea as Assessed by OCT from Baseline Over Time by Cohort - EDC	74
Table 73. Summary of Changes in EZ Line Extending +/- 5 Degrees from Fovea as Assessed by OCT from Baseline Over Time by Cohort – EDC (Only cohorts with data will be included)	74
Table 74. Summary of Changes in EZ Line Width Within Central 5mm as Assessed by OCT (Horizontal) from Baseline Over Time by Cohort - MERIT	75
Table 75. Summary of Changes in EZ Line Width Within Central 5mm as Assessed by OCT (Vertical) from Baseline Over Time by Cohort - MERIT	75
Table 76. Summary of Changes in Mean Retinal Thickness as Assessed by OCT (Horizontal) from Baseline Over Time by Cohort - MERIT	75
Table 77. Summary of Changes in Mean Retinal Thickness as Assessed by OCT (Vertical) from Baseline Over Time by Cohort - MERIT	75
Table 78. Summary of Changes in Foveal EZ Line as Assessed by OCT from Baseline Over Time by Cohort – MERIT	75
Table 79. Summary of Changes in OCT Bleb Mean Retinal Thickness from Baseline Over Time by Cohort - MERIT	75
Table 80. Summary of Changes in NEI VFQ-25 Composite and Sub-scale Scores from Baseline Over Time by Cohort (Cohorts 1-4)	76
Table 81. Summary of Changes in CVAQC Composite and Subscale Scores from Baseline Over Time for Cohort 5	78
Table 82. Summary of PECV Questionnaire Over Time by Cohort	80

Table 1. Subject Disposition by Cohort

Disposition	Cohort 1 (N=X) N (%)^a	Cohort 2 (N=X) N (%)^a	Cohort 3 (N=X) N (%)^a	Cohort 4 (N=X) N (%)^a	Cohort 5 (N=X) N (%)^a	Total (N=X) N (%)^a
Screened population						x
Safety population^b	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Discontinued Study among Safety Population^c	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Reason						
Completed	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Adverse event	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Poor compliance to protocol	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Study terminated by sponsor	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)

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Column header counts are the number of enrolled subjects in each cohort and overall. Percentages are rounded to the nearest whole number.

^b Denominators are the number of enrolled subjects in each cohort and overall.

^c Denominators are the number of subjects in the safety population in each cohort and overall.

Table 2. Summary of Demographics by Cohort

Demographic Characteristic	Cohort 1 (N=X)^a	Cohort 2 (N=X)^a	Cohort 3 (N=X)^a	Cohort 4 (N=X)^a	Cohort 5 (N=X)^a	Total (N=X)^a
Age (years)						
N	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)
Median	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)
Gender, N(%)						
Male	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Female	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Race, N(%)						
American Indian or Alaska 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 or African American	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Native Hawaiian or Other 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)
Not Reported	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)
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)
Not Reported	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)
Baseline Height (cm)						
N	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)
Median	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)

Table 2. Summary of Demographics by Cohort (continued)

Demographic Characteristic	Cohort 1 (N=X)^a	Cohort 2 (N=X)^a	Cohort 3 (N=X)^a	Cohort 4 (N=X)^a	Cohort 5 (N=X)^a	Total (N=X)^a
Baseline Weight (kg)						
N	x	x	x	x	x	x
Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
Median	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
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)
Baseline BMI (kg/m²)						
N	x	x	x	x	x	x
Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
Median	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
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)

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Column header counts and denominators are the number of subjects in the safety population in each cohort and overall. Percentages are rounded to the nearest whole number.

Table 3. Summary of Medical History by Cohort

MedDRA System Organ Class/Preferred Term^a	Cohort 1 (N=X) N (%)^b	Cohort 2 (N=X) N (%)^b	Cohort 3 (N=X) N (%)^b	Cohort 4 (N=X) N (%)^b	Cohort 5 (N=X) N (%)^b	Total (N=X) N (%)^b
SOC1	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
PT 1	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
PT2	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
...						
SOC2	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
PT1	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
PT2	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
...						
SOC3	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
PT1	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
PT2	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
...						

... Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a MedDRA Version XX.

^b Column header counts and denominators are the number of subjects in the safety population in each cohort and overall. Percentages are rounded to the nearest whole number.

Table 4. Summary of Treatment Exposure and Compliance by Cohort

	Cohort 1 (N=X)^a	Cohort 2 (N=X)^a	Cohort 3 (N=X)^a	Cohort 4 (N=X)^a	Cohort 5 (N=X)^a	Total (N=X)^a
Was full 300µL dose administered? N(%)^a						
Yes	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
<i>Reason</i>						
Reflux	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)
Dose Administered (µL)						
N	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)
Median	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)

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

^a Column header counts and denominators are the number of subjects in the safety population in each cohort and overall. Percentages are rounded to the nearest whole number.

Table 5. Summary of Concomitant Medications by WHO Drug Classification and Cohort

WHO Drug Code Level 1/ WHO Drug Code Level 2^a	Cohort 1 (N=X) N (%)^b	Cohort 2 (N=X) N (%)^b	Cohort 3 (N=X) N (%)^b	Cohort 4 (N=X) N (%)^b	Cohort 5 (N=X) N (%)^b	Total (N=X) N (%)^b
Total	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
ATC1 – 1	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
ATC2 – 1	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
ATC2 – 2	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
....						
ATC1 – 2	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
ATC2 – 1	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
ATC2 – 2	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
....						
...						

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a WHO Drug Dictionary version XX.

^b Column header counts and denominators are the number of subjects in the safety population in each cohort and overall. Percentages are rounded to the nearest whole number.

Table 6. Summary of Protocol Deviations by Cohort

	Cohort 1 (N=X)		Cohort 2 (N=X)		Cohort 3 (N=X)		Cohort 4 (N=X)		Cohort 5 (N=X)		Total (N=X)	
	Subjects with Events	# of Events	Subjects with Events	# of Events	Subjects with Events	# of Events	Subjects with Events	# of Events	Subjects with Events	# of Events	Subjects with Events	# of Events
	N (%) ^a	N	N (%) ^a	N	N (%) ^a	N	N (%) ^a	N	N (%) ^a	N	N (%) ^a	N
Total	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x
Deviation Category												
Category 1	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x
Category 2	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x
...												
Deviation Coded Term												
Term 1	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x
Term 2	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x
...												

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Column header counts and denominators are the number of subjects in the safety population in each cohort and overall. Percentages are rounded to the nearest whole number.

Table 7. Overview of TEAEs by Cohort

	Cohort 1		Cohort 2		Cohort 3		Cohort 4		Cohort 5		Total	
	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N
Any TEAE	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Any serious TEAE	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Any AESI	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Any severe TEAE	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Any TEAE leading to death	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Any TEAE leading to permanent treatment discontinuation	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Any related TEAE ^b	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Severity												
Grade 1	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Grade 2	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Grade 3	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Grade 4	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Grade 5	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Related to IMP												
Related	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Not Related	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Related to NIMP												
Related	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Not Related	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Related to Study Procedures												
Related	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Not Related	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 7. Overview of TEAEs by Cohort (continued)

	Cohort 1		Cohort 2		Cohort 3		Cohort 4		Cohort 5		Total	
	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N
Related to Surgical Procedure												
Related	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Not Related	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Outcome												
Recovered/Resolved	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Recovered/Resolved with	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Sequalae	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Recovering/Resolving	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Not Recovered/Not Resolved	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Fatal	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Unknown												

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Denominators are the number of subjects in the safety population in each cohort and overall. Percentages are rounded to the nearest whole number.

^b Related to IMP, NIMP, study procedures, and/or surgical procedure.

Table 8. Summary of TEAEs by System Organ Class, Preferred Term, Severity, and Cohort

MedDRA SOC/ PT/ Severity ^{a,b}	Cohort 1		Cohort 2		Cohort 3		Cohort 4		Cohort 5		Total	
	Subjects with Events	# of Events	Subjects with Events	# of Events	Subjects with Events	# of Events	Subjects with Events	# of Events	Subjects with Events	# of Events	Subjects with Events	# of Events
	n/N (%) ^c	N	n/N (%) ^c	N	n/N (%) ^c	N	n/N (%) ^c	N	n/N (%) ^c	N	n/N (%) ^c	N
Total	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
SOC1	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
PT1	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Grade 1	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	x/x (x)	x	x/x (x)	x
PT2	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Grade 1	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	x/x (x)	x	x/x (x)	x
SOC2	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
PT1	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Grade 1	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	x/x (x)	x	x/x (x)	x
PT2	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Grade 1	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	x/x (x)	x	x/x (x)	x
...												

Abbreviations: SOC-System Organ Class, PT-Preferred Term

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.^a MedDRA version XX.^b System organ classes are presented in descending order of number of events reported; preferred term within each system organ class are also presented in descending order of number of events reported.^c Denominators are the number of subjects in the safety population in each cohort and overall. Percentages are rounded to the nearest whole number.

Table 9. Summary of TEAEs Related to IMP by System Organ Class, Preferred Term, Severity, and Cohort

This table will be similar to Table 8.

Table 10. Summary of TEAEs Related to NIMP by System Organ Class, Preferred Term, Severity, and Cohort

This table will be similar to Table 8.

Table 11. Summary of TEAEs Related to Study Procedures by System Organ Class, Preferred Term, Severity, and Cohort

This table will be similar to Table 8.

Table 12. Summary of TEAEs Related to Surgical Procedure by System Organ Class, Preferred Term, Severity, and Cohort

This table will be similar to Table 8.

Table 13. Overview of Serious TEAEs by Cohort

This table will be similar to Table 8. The denominators will be the number of subjects in the safety population with a serious TEAE.

Table 14. Summary of Serious TEAEs by System Organ Class, Preferred Term, Severity, and Cohort

This table will be similar to Table 8. The denominators will be the number of subjects in the safety population with a serious TEAE.

Table 15. Summary of Serious TEAEs Related to Surgical Procedure by System Organ Class, Preferred Term, Severity, and Cohort

This table will be similar to Table 8. The denominators will be the number of subjects in the safety population with a serious TEAE.

Table 16. Summary of AESIs by System Organ Class, Preferred Term, and Cohort

MedDRA SOC/ PT ^{a,b}	Cohort 1		Cohort 2		Cohort 3		Cohort 4		Cohort 5		Total	
	Subjects with Events n/N (%) ^c	# of Events N	Subjects with Events n/N (%) ^c	# of Events N	Subjects with Events n/N (%) ^c	# of Events N	Subjects with Events n/N (%) ^c	# of Events N	Subjects with Events n/N (%) ^c	# of Events N	Subjects with Events n/N (%) ^c	# of Events N
Total	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
SOC1	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
PT1	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
PT2	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	x/x (x)	x	x/x (x)	x
SOC2	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
PT1	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
PT2	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	x/x (x)	x	x/x (x)	x
...												

Abbreviations: SOC-System Organ Class, PT-Preferred Term

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.^a MedDRA version XX.^b System organ classes are presented in descending order of number of events reported; preferred term within each system organ class are also presented in descending order of number of events reported.^c Denominators are the number of subjects in the safety population in each cohort and overall with an AESI. Percentages are rounded to the nearest whole number.

Table 17. Summary of Slit Lamp Assessments Over Time by Cohort - Anterior Chamber

Visit	Baseline	Post Baseline	Cohort 1 n/N (%) ^a		Cohort 2 n/N (%) ^a		Cohort 3 n/N (%) ^a		Cohort 4 n/N (%) ^a		Cohort 5 n/N (%) ^a		Total n/N (%) ^a	
			Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye
Day 2	None	None	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)
		Faint	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)
		Moderate	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)
		Marked	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)
		Intense	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)
	Faint	None	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)
		Faint	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)
		Moderate	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)
		Marked	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)
		Intense	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)
	Moderate	None	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)
		Faint	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)
		Moderate	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)
		Marked	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)
		Intense	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)
	Marked	None	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)
		Faint	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)
		Moderate	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)
		Marked	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)
		Intense	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)
	Intense	None	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)
		Faint	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)
		Moderate	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)
		Marked	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)
		Intense	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)
	...													
	...													

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Denominators are the number of subjects in the safety population in each cohort and overall with data at the given visit. Percentages are rounded to the nearest whole number.

Table 18. Summary of Ophthalmoscopy Assessments Over Time by Cohort – Macula

Visit	Baseline	Post Baseline	Cohort 1 n/N (%) ^a		Cohort 2 n/N (%) ^a		Cohort 3 n/N (%) ^a		Cohort 4 n/N (%) ^a		Cohort 5 n/N (%) ^a		Total n/N (%) ^a	
			Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye
Day 2	Normal	Normal	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)
		Abnormal, NCS	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)
		Abnormal, CS	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)
	Abnormal, NCS	Normal	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)
		Abnormal, NCS	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)
		Abnormal, CS	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)
	Abnormal, CS	Normal	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)
		Abnormal, NCS	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)
		Abnormal, CS	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)
Day 3	Normal	Normal	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)
		Abnormal, NCS	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)
		Abnormal, CS	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)
	Abnormal, NCS	Normal	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)
		Abnormal, NCS	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)
		Abnormal, CS	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)
	Abnormal, CS	Normal	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)
		Abnormal, NCS	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)
		Abnormal, CS	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: NCS = not clinically significant, CS = clinically significant

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.^a Denominators are the number of subjects in the safety population in each cohort and overall with data at the given visit. Percentages are rounded to the nearest whole number.

Table 19. Summary of Ophthalmoscopy Assessments Over Time by Cohort – Vitreous

[illegible]

Table 19. Summary of Ophthalmoscopy Assessments Over Time by Cohort – Vitreous (continued)

Visit	Baseline	Post Baseline	Cohort 1		Cohort 2		Cohort 3		Cohort 4		Cohort 5		Total	
			n/N (%) ^a		n/N (%) ^a		n/N (%) ^a		n/N (%) ^a		n/N (%) ^a		n/N (%) ^a	
			Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye

...

Abbreviations: ONH = optic nerve head (optic disc)

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.^a Denominators are the number of subjects in the safety population in each cohort and overall with data at the given visit. Percentages are rounded to the nearest whole number.

Table 20. Summary of IOP (mmHg) Over Time by Cohort

Visit	Cohort 1		Cohort 2		Cohort 3		Cohort 4		Cohort 5		Total	
	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye
Baseline												
N	x	x	x	x	x	x	x	x	x	x	x	x
Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
Median	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
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)	(x.x, x.x)	(x.x, x.x)
Day 2												
N	x	x	x	x	x	x	x	x	x	x	x	x
Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
Median	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
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)	(x.x, x.x)	(x.x, x.x)
...												
...												

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

Table 21. Summary of Changes in IOP (mmHg) from Baseline Over Time by Cohort

This table will be similar to Table 20.

Table 22. Summary of Subjects with Post-baseline PCSAs in Laboratory Parameters by Cohort

Laboratory Parameter	PCSA Criteria	Cohort 1 n/N (%) ^a	Cohort 2 n/N (%) ^a	Cohort 3 n/N (%) ^a	Cohort 4 n/N (%) ^a	Cohort 5 n/N (%) ^a	Total n/N (%) ^a
Chemistry							
Albumin (g/L)	≤ 25 g/L	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Alkaline Phosphate (IU/L)	> 1.5 ULN	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Alanine Aminotransferase (IU/L)	> 3 ULN	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Aspartate Aminotransferase (IU/L)	> 3 ULN	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Total Bilirubin (umol/L)	> 1.5 ULN	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Urea Nitrogen (mmol/L)	≥ 17 mmol/L	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Cholesterol (mmol/L)	≥ 7.74 mmol/L	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Creatine Kinase (IU/L)	> 3 ULN	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Chloride (mmol/L)	< 80 mmol/L	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
	> 115 mmol/L	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Creatinine (umol/L)	≥ 150 umol/L (Adults)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
	≥ 30% change from baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Glucose (mmol/L)	≤ 3.9 mmol/L and < LLN	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
	≥ 11.1 mmol/L (unfasted); ≥ 7 mmol/L (fasted)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Potassium (mmol/L)	< 3 mmol/L	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
	≥ 5.5 mmol/L	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Sodium (mmol/L)	≤ 129 mmol/L	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
	≥ 160 mmol/L	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Triglycerides (mmol/L)	≥ 4.6 mmol/L	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Hematology							
Basophils (10/L)	> 0.1 * 10 ⁹ /L	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Eosinophils (10/L)	> 0.5 * 10 ⁹ /L or > ULN (if ULN ≥ 0.5 * 10 ⁹ /L)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Hematocrit (v/v)	≤ 0.37 v/v (Male); ≤ 0.32 v/v (Female)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
	≥ 0.55 v/v (Male); ≥ 0.5 v/v (Female)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Hemoglobin (g/L)	≤ 115 g/L (Male); ≤ 95 g/L (Female)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
	≥ 185 g/L (Male); ≥ 165 g/L (Female)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
	Decrease from baseline ≥ 20 g/L	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Lymphocytes (10/L)	> 4 * 10 ⁹ /L	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)

Table 22. Summary of Subjects with Post-baseline PCSAs in Laboratory Parameters by Cohort (continued)

Laboratory Parameter	PCSA Criteria	Cohort 1 n/N (%) ^a	Cohort 2 n/N (%) ^a	Cohort 3 n/N (%) ^a	Cohort 4 n/N (%) ^a	Cohort 5 n/N (%) ^a	Total n/N (%) ^a
Monocytes (10/L)	$> 0.7 * 10^9/L$	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Neutrophils (10/L)	$< 1.5 * 10^9/L$ (Non-Black); $< 1 * 10^9/L$ (Black)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Platelet Count (10/L)	$< 100 * 10^9/L$	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
	$\geq 700 * 10^9/L$	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Erythrocyte Count (RBC) (10/L)	$\geq 6 * 10^{12}/L$	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Leukocyte Count (WBC)	$< 3 * 10^9/L$ (Non-Black); $< 2 * 10^9/L$ (Black)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
	$\geq 16 * 10^9/L$	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)

Abbreviations: PCSA = Potentially clinically significant abnormalities

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

The number (n) represents the number of subjects in each cohort and overall, who met the criterion in question at least once during the TEAE period. The denominator, N, is the number of subjects in each cohort and overall, who had that parameter assessed during the TEAE period.

For PCSA including conditions based only on change from baseline, the denominator is restricted to subjects having a baseline and at least one post-baseline value during the TEAE period.

For PCSA including conditions based on the value and change from baseline, in the case of missing baseline or baseline emergent, the PCSA criteria will be restricted to the threshold based on values during the TEAE period only, and the denominator is restricted for subjects having at least one value during the TEAE period.

Percentages are rounded to the nearest whole number.

Table 23. Summary of Subjects with Post-Treatment Hematology Laboratory Parameters Outside of Normal Range by Cohort

Laboratory Parameter^a	Cohort 1 n/N (%)^b	Cohort 2 n/N (%)^b	Cohort 3 n/N (%)^b	Cohort 4 n/N (%)^b	Cohort 5 n/N (%)^b	Total n/N (%)^b
Activated Partial Thromboplastin Time (sec)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Basophils (10⁹/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Eosinophils (10⁹/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Hematocrit (v/v)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Hemoglobin (g/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Prothrombin Intl. Normalized Ratio						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Lymphocytes (10⁹/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Monocytes (10⁹/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Neutrophils (10⁹/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Platelets (10⁹/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Erythrocytes (10¹²/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)

Table 23. Summary of Subjects with Post-Treatment Hematology Laboratory Parameters Outside of Normal Range by Cohort
(continued)

Laboratory Parameter^a	Cohort 1 n/N (%)^b	Cohort 2 n/N (%)^b	Cohort 3 n/N (%)^b	Cohort 4 n/N (%)^b	Cohort 5 n/N (%)^b	Total n/N (%)^b
Leucocytes (10⁹/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Subjects are counted as Within Normal Range for a laboratory parameter if all post-treatment values are within normal range. Subjects are counted as Outside of Normal Range for a laboratory parameter if at least one post-treatment value is outside of normal range.

^b Denominators are the number of subjects in the safety population with hematology laboratory data. Percentages are rounded to the nearest whole number.

Table 24. Summary of Subjects with Post-Treatment Chemistry Parameters Outside of Normal Range by Cohort

Laboratory Parameter^a	Cohort 1 n/N (%)^b	Cohort 2 n/N (%)^b	Cohort 3 n/N (%)^b	Cohort 4 n/N (%)^b	Cohort 5 n/N (%)^b	Total n/N (%)^b
Albumin (g/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Alkaline Phosphate (IU/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Alanine Aminotransferase (IU/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Aspartate Aminotransferase (IU/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Direct Bilirubin (umol/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Bilirubin (umol/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Blood Urea Nitrogen (mmol/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Calcium (mmol/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Cholesterol (mmol/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Creatine Kinase^c						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Chloride (mmol/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)

Table 24. Summary of Subjects with Post-Treatment Chemistry Parameters Outside of Normal Range by Cohort (continued)

Laboratory Parameter^a	Cohort 1 n/N (%)^b	Cohort 2 n/N (%)^b	Cohort 3 n/N (%)^b	Cohort 4 n/N (%)^b	Cohort 5 n/N (%)^b	Total n/N (%)^b
Creatinine (umol/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Gamma Glutamyl Transferase (IU/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Glucose (mmol/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Potassium (mmol/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Protein (g/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Sodium (mmol/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Triglycerides (mmol/L)						
Within Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Outside of Normal Range	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

^a Subjects are counted as Within Normal Range for a laboratory parameter if all post-treatment values are within normal range. Subjects are counted as Outside of Normal Range for a laboratory parameter if at least one post-treatment value is outside of normal range.

^b Denominators are the number of subjects in the safety population with chemistry laboratory data. Percentages are rounded to the nearest whole number.

^c Creatine Kinase is measured in mg/dL for UPenn subjects and in IU/L for OHSU subjects.

Table 25. Summary of ADA AAV5 and RetGC1 Results Over Time by Cohort

Visit^a	Cohort 1 n/N (%)^b	Cohort 2 n/N (%)^b	Cohort 3 n/N (%)^b	Cohort 4 n/N (%)^b	Cohort 5 n/N (%)^b	Total n/N (%)^b
Baseline						
<i>AAV5</i>						
Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Negative	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
<i>RetGC1</i>						
Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Negative	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Day 28						
<i>AAV5</i>						
Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Negative	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
<i>RetGC1</i>						
Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Negative	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
...						

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

^a subject is considered to be positive if screen result and titer are positive or screen result is putative and confirm result and titer are positive at the respective visit. A subject is considered negative if the screen result, confirm result, and/or titer are negative at the respective visit.

^b Denominators are the number of subjects in each cohort and overall with ADA results at the specified visit. Percentages are rounded to the nearest whole number.

Table 26. Summary of ELISpot to AAV5 Results Over Time by Cohort

Visit^a	Cohort 1 n/N (%)^b	Cohort 2 n/N (%)^b	Cohort 3 n/N (%)^b	Cohort 4 n/N (%)^b	Cohort 5 n/N (%)^b	Total n/N (%)^b
Baseline						
Detected	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Not Detected	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
No Result	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Day 28						
Detected	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Not Detected	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
No Result	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)

...

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

^a subject is considered to have a detected result if at least one of the pools tested had a detected result. A subject is considered to have a not detected result if all pools tested had a not detected result. A subject is considered to have no result if the result cannot be assessed for any reason (eg, insufficient sample quantity).

^b Denominators are the number of subjects in each cohort and overall with ELISpot to AAV5 results at the specified visit. Percentages are rounded to the nearest whole number.

Table 27. Summary of ELISpot to RetGC1 Results Over Time by Cohort

This table will be similar to Table 26.

Table 28. Summary of Treatment-Emergent ADA Positivity Over Time by Cohort

Visit^a	Cohort 1 n/N (%)^b	Cohort 2 n/N (%)^b	Cohort 3 n/N (%)^b	Cohort 4 n/N (%)^b	Cohort 5 n/N (%)^b	Total n/N (%)^b
Day 28						
<i>AAV5</i>						
Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Not Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
<i>RetGC1</i>						
Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Not Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 12						
<i>AAV5</i>						
Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Not Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
<i>RetGC1</i>						
Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Not Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
...						

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Treatment-emergent positivity is defined as: 1) a post-baseline result that is positive when the baseline result is negative or 2) a post-baseline result that has a titer greater than or equal to 4 times the baseline titer when the baseline result is positive, while titer values are available at both baseline and post-baseline visits.

^b Denominators are the number of subjects in the safety population in each cohort and overall with ADA results at the specified visit. Percentages are rounded to the nearest whole number.

Table 29. Summary of Treatment-Emergent ELISpot Positivity Over Time by Cohort

Visit ^a	Cohort 1 n/N (%) ^b	Cohort 2 n/N (%) ^b	Cohort 3 n/N (%) ^b	Cohort 4 n/N (%) ^b	Cohort 5 n/N (%) ^b	Total n/N (%) ^b
Day 28						
<i>AAV5</i>						
Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Not Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
N/A	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
<i>RetGC1</i>						
Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Not Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
N/A	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 12						
<i>AAV5</i>						
Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Not Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
N/A	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
<i>RetGC1</i>						
Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Not Positive	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
N/A	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)

...

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.^a Treatment-emergent positivity is defined as a post-baseline result that has a fold increase of ≥ 2 relative to baseline. A subject is considered to have an N/A result when treatment-emergent positivity cannot be assessed for any reason (e.g., insufficient sample quantity) at the specified visit.^b Denominators are the number of subjects in the safety population in each cohort and overall with ELISpot results at the specified visit. Percentages are rounded to the nearest whole number.

Table 30. Summary of AESIs by Baseline ADA Assay Result

ADA Assay	Cohort 1		Cohort 2		Cohort 3		Cohort 4		Cohort 5		Total	
	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N
<i>AAV5</i>												
Positive at Baseline	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Negative at Baseline	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
<i>RetGC1</i>												
Positive at Baseline	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Negative at Baseline	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	xx (x)	x

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Denominators are the number of subjects in the safety population in each cohort and overall with an AESI. Percentages are rounded to the nearest whole number.

Table 31. Summary of SAEs by Baseline ADA Assay Result

This table will be similar to Table 30.

Table 32. Summary of AESIs by Baseline ELISpot Assay Result

	Cohort 1		Cohort 2		Cohort 3		Cohort 4		Cohort 5		Total	
	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N
ADA Assay												
<i>AAV5</i>												
Detected at Baseline	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Not Detected at Baseline	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
No Result at Baseline	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
<i>RetGCI</i>												
Detected at Baseline	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Not Detected at Baseline	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
No Result at Baseline	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Denominators are the number of subjects in the safety population in each cohort and overall with an AESI. Percentages are rounded to the nearest whole number.

Table 33. Summary of SAEs by Baseline ELISpot Assay Result

This table will be similar to Table 32.

Table 34. Summary of AESIs by Treatment-emergent ADA Assay

ADA Assay	Cohort 1		Cohort 2		Cohort 3		Cohort 4		Cohort 5		Total	
	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N
<i>AAV5</i>												
Positive treatment-emergent	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
No positive treatment-emergent	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
<i>RetGC1</i>												
Positive treatment-emergent	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
No positive treatment-emergent	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Denominators are the number of subjects in the safety population in each cohort and overall with an AESI. Percentages are rounded to the nearest whole number.

Table 35. Summary of SAEs by Treatment-emergent ADA Assay

This table will be similar to Table 34.

Table 36. Summary of AESIs by Treatment-emergent ELISpot Assay

This table will be similar to Table 34.

Table 37. Summary of SAEs by Treatment-emergent ELISpot Assay

This table will be similar to Table 34.

Table 38. Summary of Heart Rate Over Time by Cohort

Visit	Heart Rate (beats/min)						Change from Baseline (beats/min) ^a					
	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Total	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Total
Baseline												
N	x	x	x	x	x	x						
Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)						
Median	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx						
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)						
Day 1												
N	x	x	x	x	x	x						
Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)						
Median	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx						
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)						
Day 2												
N	x	x	x	x	x	x	x	x	x	x	x	x
Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
Median	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
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)	(x.x, x.x)	(x.x, x.x)
...												
...												

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a For vital signs, the baseline value is the value taken at the Day 1 pre-dose assessment.

Table 39. Summary of Systolic Blood Pressure Over Time by Cohort

This table will be similar to Table 38.

Table 40. Summary of Diastolic Blood Pressure Over Time by Cohort

This table will be similar to Table 38.

Table 41. Summary of Subjects with PCSAs in Vital Signs by Cohort

This table will be similar to Table 22.

Table 42. Summary of Adverse Events by Follow-up Period and Cohort

Follow-up Period	Cohort 1		Cohort 2		Cohort 3		Cohort 4		Cohort 5		Total	
	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N	Subjects with Events n/N (%) ^a	# of Events N
Weeks 0-52	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Weeks 53-104	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Weeks 105-156	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Weeks 157-208	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Weeks 52-260	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x
Weeks 0-260	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x	x/x (x)	x

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Denominators are the number of subjects in the safety population in each cohort and overall. Percentages are rounded to the nearest whole number.

Table 43. Summary of Serious Adverse Events by Follow-up Period and Cohort

This table will be similar to Table 42.

Table 44. Summary of AESIs by Follow-up Period and Cohort

This table will be similar to Table 42.

Table 45. Summary of Changes in FST (decibels) Over Time by Cohort– Red, Light Adapted (All Sites)

Visit	Cohort 1		Cohort 2		Cohort 3		Cohort 4		Cohort 5		Total	
	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye
Day 3												
N	x	x	x	x	x	x	x	x	x	x	x	x
Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
Median	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
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)	(x.x, x.x)	(x.x, x.x)
...												
...												
All Visits ^a												
N	x	x	x	x	x	x	x	x	x	x	x	x
Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
Median	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
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)	(x.x, x.x)	(x.x, x.x)

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

^a Includes all visits from Day 28 and after.

Table 46. Summary of Changes in FST (decibels) Over Time by Cohort– Red, Dark Adapted (All Sites)

This table will be similar to Table 45.

Table 47. Summary of Changes in FST (decibels) Over Time by Cohort– White, Light Adapted (All Sites)

This table will be similar to Table 45.

Table 48. Summary of Changes in FST (decibels) Over Time by Cohort– White, Dark Adapted (All Sites)

This table will be similar to Table 45.

Table 49. Summary of Changes in FST (decibels) Over Time by Cohort– Blue, Light Adapted (All Sites)

This table will be similar to Table 45.

Table 50. Summary of Changes in FST (decibels) Over Time by Cohort– Blue, Dark Adapted (All Sites)

This table will be similar to Table 45.

Table 51. Summary of Difference in Change from Baseline in FST (decibels) Between the Treated and Untreated Eyes Over Time by Cohort – Red, Light Adapted (All Sites)

Visit	Difference in Change from Baseline Between Eyes (dB) ^a					Total
	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	
Day 1						
N	x	x	x	x	x	x
Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
Median	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
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)
...						
...						
Day 28						
N	x	x	x	x	x	x
Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
Median	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
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)
...						
...						
All Visits^b						
N	x	x	x	x	x	x
Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
Median	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
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)

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

^a Difference is calculated as treated eye – untreated eye.

^b Includes all visits from Day 28 and after.

Table 52. Summary of Difference in Change from Baseline FST (decibels) Between the Treated and Untreated Eyes Over Time by Cohort – Red, Dark Adapted (All Sites)

This table will be similar to Table 51.

Table 53. Summary of Difference in Change from Baseline FST (decibels) Between the Treated and Untreated Eyes Over Time by Cohort – White, Light Adapted (All Sites)

This table will be similar to Table 51.

Table 54. Summary of Difference in Change from Baseline FST (decibels) Between the Treated and Untreated Eyes Over Time by Cohort – White, Dark Adapted (All Sites)

This table will be similar to Table 51.

Table 55. Summary of Difference in Change from Baseline FST (decibels) Between the Treated and Untreated Eyes Over Time by Cohort – Blue, Light Adapted (All Sites)

This table will be similar to Table 51.

Table 56. Summary of Difference in Change from Baseline FST (decibels) Between the Treated and Untreated Eyes Over Time by Cohort – Blue, Dark Adapted (All Sites)

This table will be similar to Table 51.

Table 57. FST (decibels) Analysis Results – Dark Adapted

Cohort	Stimulus Color	Visit	Treated Eye Δ		Untreated Eye Δ		Difference in Δ^b		p-value ^c
			N ^a	Mean (SD)	N ^a	Mean (SD)	N ^a	Mean (SD)	
Cohort 1	Blue	Day 28	x	x.xx (x.xx)	x	x.xx (x.xx)	x	x.xx (x.xx)	x.xx
		...	x	x.xx (x.xx)	x	x.xx (x.xx)	x	x.xx (x.xx)	x.xx
		All Visits ^d	x	x.xx (x.xx)	x	x.xx (x.xx)	x	x.xx (x.xx)	x.xx
	Red	...	x	x.xx (x.xx)	x	x.xx (x.xx)	x	x.xx (x.xx)	x.xx
		...	x	x.xx (x.xx)	x	x.xx (x.xx)	x	x.xx (x.xx)	x.xx
	White	...	x	x.xx (x.xx)	x	x.xx (x.xx)	x	x.xx (x.xx)	x.xx
		...	x	x.xx (x.xx)	x	x.xx (x.xx)	x	x.xx (x.xx)	x.xx
Cohort 2	...	...	x	x.xx (x.xx)	x	x.xx (x.xx)	x	x.xx (x.xx)	x.xx
		...	x	x.xx (x.xx)	x	x.xx (x.xx)	x	x.xx (x.xx)	x.xx
Cohort 3	...	...	x	x.xx (x.xx)	x	x.xx (x.xx)	x	x.xx (x.xx)	x.xx
		...	x	x.xx (x.xx)	x	x.xx (x.xx)	x	x.xx (x.xx)	x.xx
Cohort 4	...	...	x	x.xx (x.xx)	x	x.xx (x.xx)	x	x.xx (x.xx)	x.xx
		...	x	x.xx (x.xx)	x	x.xx (x.xx)	x	x.xx (x.xx)	x.xx
Cohort 5	...	...	x	x.xx (x.xx)	x	x.xx (x.xx)	x	x.xx (x.xx)	x.xx
		...	x	x.xx (x.xx)	x	x.xx (x.xx)	x	x.xx (x.xx)	x.xx
High Dose	...	...	x	x.xx (x.xx)	x	x.xx (x.xx)	x	x.xx (x.xx)	x.xx
		...	x	x.xx (x.xx)	x	x.xx (x.xx)	x	x.xx (x.xx)	x.xx

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

High Dose includes subjects from Cohorts 3, 4, and 5.

Δ indicates change from baseline.

Abbreviation: NE - Not Estimable; SD - standard deviation

Yellow highlighting corresponds to p-values that demonstrate significance at the 0.05 level.

^a Number of observations.

^b Difference in the change from baseline between the treated and untreated eyes.

^c For individual visits, p-value is from t-test used to compare the difference in the change from baseline between the treated and untreated eyes. For all visits, p-value is from generalized estimating equation used to compare the difference in the change from baseline between the treated and untreated eyes. P-values are rounded to two decimal places.

^d Includes all visits from Day 28 and after. Standard error is presented as SD in difference in change column.

Table 58. FST (decibels) Analysis Results – Light Adapted

This table will be similar to Table 57.

Table 59. Summary of BCVA (logMAR) Over Time by Cohort

This table will be similar to Table 45 and will include the Baseline.

Table 60. Summary of BCVA (ETDRS letters) Over Time by Cohort

This table will be similar to Table 45 and will include the Baseline.

Table 61. Summary of Changes in BCVA (logMAR) from Baseline Over Time by Cohort

This table will be similar to Table 45.

Table 62. Summary of Changes in BCVA (ETDRS letters) from Baseline Over Time by Cohort

This table will be similar to Table 45.

Table 63. Summary of Difference in BCVA (logMAR) Between the Treated and Untreated Eyes Over Time by Cohort

This table will be similar to Table 51 and will include the Baseline.

Table 64. Summary of Difference in BCVA (ETDRS letters) Between the Treated and Untreated Eyes Over Time by Cohort

This table will be similar to Table 51 and will include the Baseline.

Table 65. BCVA (logMAR) Analysis Results

This table will be similar to Table 57. Column for Stimulus Color will be excluded.

Table 66. BCVA (ETDRS letters) Analysis Results

This table will be similar to Table 57. Column for Stimulus Color will be excluded.

Table 67. Summary of Changes in TPLR Response Threshold from Baseline Over Time by Cohort – Red (UPenn)

This table will be similar to Table 20.

Table 68. Summary of Changes in TPLR Response Threshold from Baseline Over Time by Cohort – Blue (UPenn)

This table will be similar to Table 20.

Table 69. Summary of Changes in Overall OCI from Baseline Over Time by Cohort – Fixation Off

This table will be similar to Table 20.

Table 70. Summary of Changes in Overall OCI from Baseline Over Time by Cohort – Fixation On

This table will be similar to Table 20.

Table 71. Summary of Changes in Photoaversion Threshold Over Time by Cohort

This table will be similar to Table 20.

Table 72. Summary of Changes in Retinal Thickness at the Fovea as Assessed by OCT from Baseline Over Time by Cohort - EDC

This table will be similar to Table 20. Only cohorts with data will be included.

Table 73. Summary of Changes in EZ Line Extending +/- 5 Degrees from Fovea as Assessed by OCT from Baseline Over Time by Cohort – EDC (Only cohorts with data will be included)

Visit	Baseline	Post Baseline	Cohort 1 n/N (%) ^a		Cohort 2 n/N (%) ^a		Cohort 3 n/N (%) ^a		Cohort 4 n/N (%) ^a		Cohort 5 n/N (%) ^a		Total n/N (%) ^a	
			Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye	Treated Eye	Untreated Eye
Day 28	Normal	Normal	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)
		Abnormal	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)
		Absent	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)
	Abnormal	Normal	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)
		Abnormal	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)
		Absent	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)
	Absent	Normal	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)
		Abnormal	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)
		Absent	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)
Week 8	Normal	Normal	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)
		Abnormal	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)
		Absent	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)
	Abnormal	Normal	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)
		Abnormal	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)
		Absent	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)
	Absent	Normal	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)
		Abnormal	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)
		Absent	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)
...														
...														

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Denominators are the number of subjects in the safety population in each cohort and overall with data at the given visit and baseline. Percentages are rounded to the nearest whole number.

Table 74. Summary of Changes in EZ Line Width Within Central 5mm as Assessed by OCT (Horizontal) from Baseline Over Time by Cohort - MERIT

This table will be similar to Table 20. Only cohorts with data will be included.

Table 75. Summary of Changes in EZ Line Width Within Central 5mm as Assessed by OCT (Vertical) from Baseline Over Time by Cohort - MERIT

This table will be similar to Table 20. Only cohorts with data will be included.

Table 76. Summary of Changes in Mean Retinal Thickness as Assessed by OCT (Horizontal) from Baseline Over Time by Cohort - MERIT

This table will be similar to Table 20. Only cohorts with data will be included.

Table 77. Summary of Changes in Mean Retinal Thickness as Assessed by OCT (Vertical) from Baseline Over Time by Cohort - MERIT

This table will be similar to Table 20. Only cohorts with data will be included.

Table 78. Summary of Changes in Foveal EZ Line as Assessed by OCT from Baseline Over Time by Cohort – MERIT

This table will be similar to Table 73. Only cohorts with data will be included.

Table 79. Summary of Changes in OCT Bleb Mean Retinal Thickness from Baseline Over Time by Cohort - MERIT

This table will be similar to Table 20. Only cohorts with data will be included.

Table 80. Summary of Changes in NEI VFQ-25 Composite and Sub-scale Scores from Baseline Over Time by Cohort (Cohorts 1-4)

Visit	Change in NEI VFQ-25 Score				
	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Total
Day 28					
<i>Composite Score</i>					
N	x	x	x	x	x
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x.x	x.x	x.x	x.x	x.x
Range (Min, Max)	(x, x)	(x, x)	(x, x)	(x, x)	(x, x)
<i>General Health</i>					
N	x	x	x	x	x
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x.x	x.x	x.x	x.x	x.x
Range (Min, Max)	(x, x)	(x, x)	(x, x)	(x, x)	(x, x)
<i>General Vision</i>					
N	x	x	x	x	x
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x.x	x.x	x.x	x.x	x.x
Range (Min, Max)	(x, x)	(x, x)	(x, x)	(x, x)	(x, x)
<i>Ocular Pain</i>					
N	x	x	x	x	x
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x.x	x.x	x.x	x.x	x.x
Range (Min, Max)	(x, x)	(x, x)	(x, x)	(x, x)	(x, x)
<i>Near Activities</i>					
N	x	x	x	x	x
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x.x	x.x	x.x	x.x	x.x
Range (Min, Max)	(x, x)	(x, x)	(x, x)	(x, x)	(x, x)
<i>Distance Activities</i>					
N	x	x	x	x	x
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x.x	x.x	x.x	x.x	x.x
Range (Min, Max)	(x, x)	(x, x)	(x, x)	(x, x)	(x, x)
<i>Social Functioning</i>					
N	x	x	x	x	x
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)

Table 80. Summary of Changes in NEI VFQ-25 Composite and Sub-scale Scores from Baseline Over Time by Cohort (Cohorts 1-4)
(continued)

Visit	Change in NEI VFQ-25 Score				
	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Total
Median	x.x	x.x	x.x	x.x	x.x
Range (Min, Max)	(x, x)	(x, x)	(x, x)	(x, x)	(x, x)
<i>Mental Health</i>					
N	x	x	x	x	x
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x.x	x.x	x.x	x.x	x.x
Range (Min, Max)	(x, x)	(x, x)	(x, x)	(x, x)	(x, x)
<i>Role Difficulties</i>					
N	x	x	x	x	x
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x.x	x.x	x.x	x.x	x.x
Range (Min, Max)	(x, x)	(x, x)	(x, x)	(x, x)	(x, x)
<i>Dependency</i>					
N	x	x	x	x	x
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x.x	x.x	x.x	x.x	x.x
Range (Min, Max)	(x, x)	(x, x)	(x, x)	(x, x)	(x, x)
<i>Driving</i>					
N	x	x	x	x	x
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x.x	x.x	x.x	x.x	x.x
Range (Min, Max)	(x, x)	(x, x)	(x, x)	(x, x)	(x, x)
<i>Color Vision</i>					
N	x	x	x	x	x
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x.x	x.x	x.x	x.x	x.x
Range (Min, Max)	(x, x)	(x, x)	(x, x)	(x, x)	(x, x)
<i>Peripheral Vision</i>					
N	x	x	x	x	x
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x.x	x.x	x.x	x.x	x.x
Range (Min, Max)	(x, x)	(x, x)	(x, x)	(x, x)	(x, x)

...

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye.

Table 81. Summary of Changes in CVAQC Composite and Subscale Scores from Baseline Over Time for Cohort 5

Visit	Change in CVAQC Score Cohort 5
Day 28	
<i>Composite</i>	
N	x
Mean (SD)	x.xxx (x.xxx)
Median	x.xxx
Range (Min, Max)	(x.xx, x.xx)
<i>Education</i>	
N	x
Mean (SD)	x.xxx (x.xxx)
Median	x.xxx
Range (Min, Max)	(x.xx, x.xx)
<i>Near Vision</i>	
N	x
Mean (SD)	x.xxx (x.xxx)
Median	x.xxx
Range (Min, Max)	(x.xx, x.xx)
<i>Distance Vision</i>	
N	x
Mean (SD)	x.xxx (x.xxx)
Median	x.xxx
Range (Min, Max)	(x.xx, x.xx)
<i>Getting Around</i>	
N	x
Mean (SD)	x.xxx (x.xxx)
Median	x.xxx
Range (Min, Max)	(x.xx, x.xx)
<i>Social Interaction</i>	
N	x
Mean (SD)	x.xxx (x.xxx)
Median	x.xxx

Table 81. Summary of Changes in CVAQC Composite and Subscale Scores from Baseline Over Time for Cohort 5 (continued)

Visit	Change in CVAQC Score
	Cohort 5
Range (Min, Max)	(x.xx, x.xx)
<i>Entertainment</i>	
N	x
Mean (SD)	x.xxx (x.xxx)
Median	x.xxx
Range (Min, Max)	(x.xx, x.xx)
<i>Sports</i>	
N	x
Mean (SD)	x.xxx (x.xxx)
Median	x.xxx
Range (Min, Max)	(x.xx, x.xx)
Week 12	
<i>Composite</i>	
N	x
Mean (SD)	x.xxx (x.xxx)
Median	x.xxx
Range (Min, Max)	(x.xx, x.xx)
...	
Cohort 5 is 1.0x10 ¹¹ vg/eye.	

Table 82. Summary of PECV Questionnaire Over Time by Cohort

Visit	Cohort 1 n/N (%)^a	Cohort 2 n/N (%)^a	Cohort 3 n/N (%)^a	Cohort 4 n/N (%)^a	Cohort 5 n/N (%)^a	Total n/N (%)^a
Day 28						
<i>Changes in vision since start of study?</i>						
Yes	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
No	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 12						
<i>Changes in vision since start of study?</i>						
Yes	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
No	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
...						
...						

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Denominators are the number of subjects in the safety population with data at the specified visit. Percentages are rounded to the nearest whole number.

APPENDIX 3. FIGURES**LIST OF FIGURES**

Figure 1. Consort Diagram	83
Figure 2. Mean IOP Over Time by Cohort	84
Figure 3. Mean Change in IOP from Baseline Over Time by Cohort	84
Figure 4. IOP Over Time by Subject	85
Figure 5. Change in IOP from Baseline Over Time by Subject	86
Figure 6. Anti-AAV5 Titer Over Time by Cohort and Subject	86
Figure 7. Anti-RetGC1 Titer Over Time by Cohort and Subject	86
Figure 8. Mean Heart Rate Values Over Time by Cohort	87
Figure 9. Mean Systolic Blood Pressure Over Time by Cohort	88
Figure 10. Mean Diastolic Blood Pressure Over Time by Cohort	88
Figure 11. Mean FST (decibels) Over Time by Cohort (UPenn)	89
Figure 12. Mean Change in FST (decibels) from Baseline Over Time by Cohort (All Sites)	89
Figure 13. Mean Change in Dark Adapted FST (decibels) from Baseline Over Time for High-Dose Cohorts (All Sites)	90
Figure 14. Mean Change in Treated Eye Dark Adapted FST (decibels) from Baseline Over Time for Cohort 1, Cohort 2, and High-Dose Cohorts (All Sites)	91
Figure 15. FST (decibels) Over Time by Subject (UPenn)	92
Figure 16. FST (decibels) Over Time by Subject (OHSU)	92
Figure 17. Change in FST (decibels) from Baseline Over Time by Subject (All Sites)	92
Figure 18. Spaghetti Plot of FST (decibels) Over Time by Subject (UPenn)	92
Figure 19. Spaghetti Plot of Change in FST (decibels) from Baseline Over Time by Subject (All Sites)	92
Figure 20. Mean BCVA (logMAR) Over Time by Cohort	92
Figure 21. Mean BCVA (ETDRS letters) Over Time by Cohort	92
Figure 22. Mean Change in BCVA (logMAR) Over Time by Cohort	92
Figure 23. Mean Change in BCVA (ETDRS letters) Over Time by Cohort	92
Figure 24. Mean Change in BCVA (logMAR) from Baseline Over Time for Cohort 1, Cohort 2, and High-Dose Cohorts	93

Figure 25. BCVA (logMAR) Over Time by Subject.....	93
Figure 26. BCVA (ETDRS letters) Over Time by Subject	93
Figure 27. Change in BCVA (logMAR) from Baseline Over Time by Subject.....	93
Figure 28. Change in BCVA (ETDRS letters) from Baseline Over Time by Subject.....	93
Figure 29. Spaghetti Plot for BCVA (logMAR) Over Time by Subject	94
Figure 30. Spaghetti Plot for Change in BCVA (logMAR) from Baseline Over Time by Subject	94
Figure 31. Mean TPLR Response Threshold Over Time by Cohort (UPenn).....	95
Figure 32. Mean Change in TPLR Response Threshold Over Time by Cohort (UPenn)	95
Figure 33. Mean Retinal Thickness at the Fovea as Assessed by OCT Over Time by Cohort - EDC	95
Figure 34. Mean Change in Retinal Thickness at the Fovea as Assessed by OCT from Baseline Over Time by Cohort - EDC.....	95
Figure 35. Mean Change in EZ Line Width Within Central 5mm as Assessed by OCT from Baseline Over Time by Cohort - MERIT	96
Figure 36. Mean Change in Mean Retinal Thickness as Assessed by OCT from Baseline Over Time by Cohort - MERIT	96
Figure 37. Mean OCT Bleb Mean Retinal Thickness Over Time by Cohort - MERIT	96
Figure 38. Mean Change in NEI VFQ-25 Composite Score from Baseline Over Time by Cohort	97
Figure 39. Mean Change in CVAQC Composite Score from Baseline Over Time for Cohort 5	97
Figure 40. Mobility Testing Scores Over Time by Subject (UPenn)	97
Figure 41. Change in Mobility Testing Scores Over Time by Subject (UPenn)	97

Figure 1. Consort Diagram

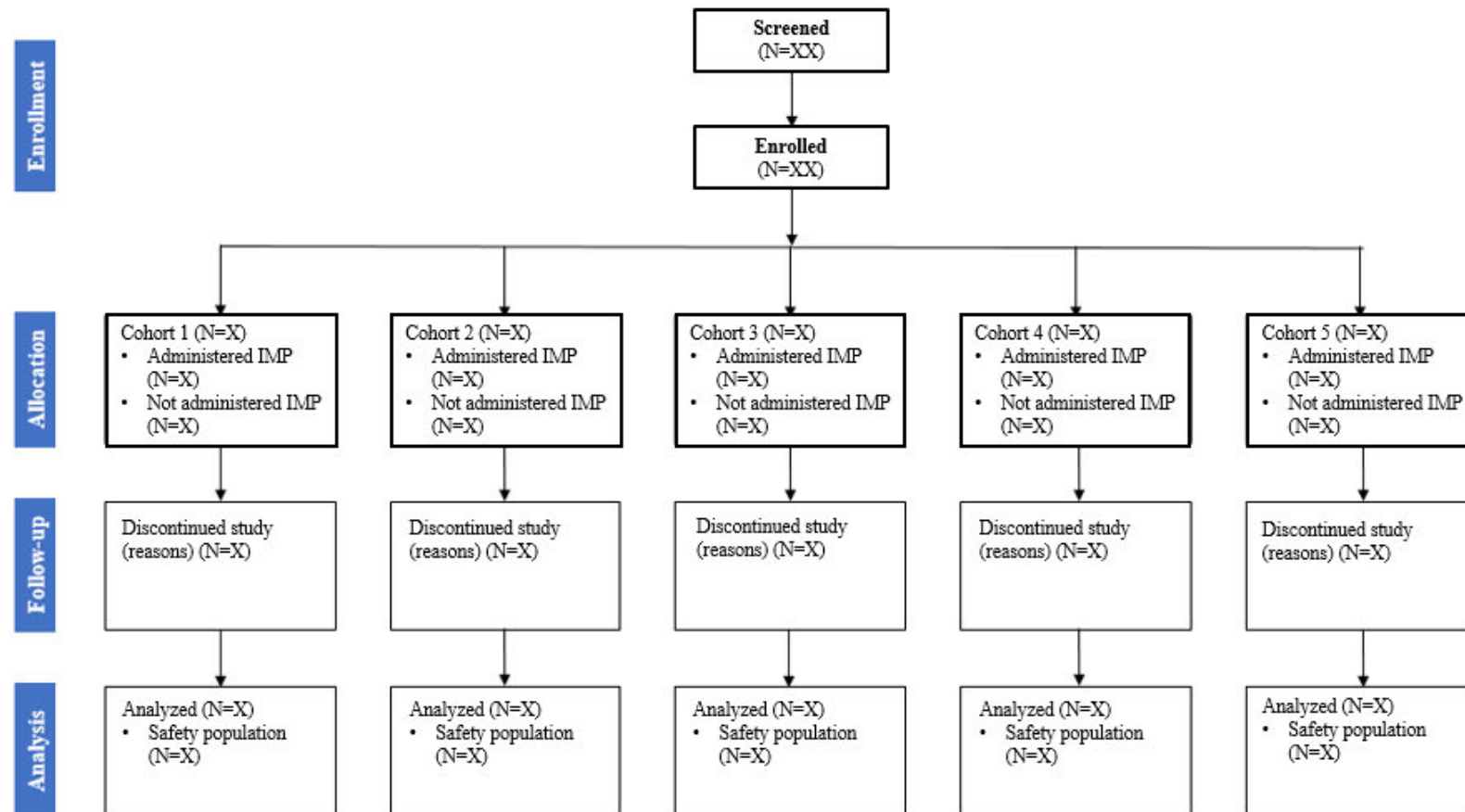
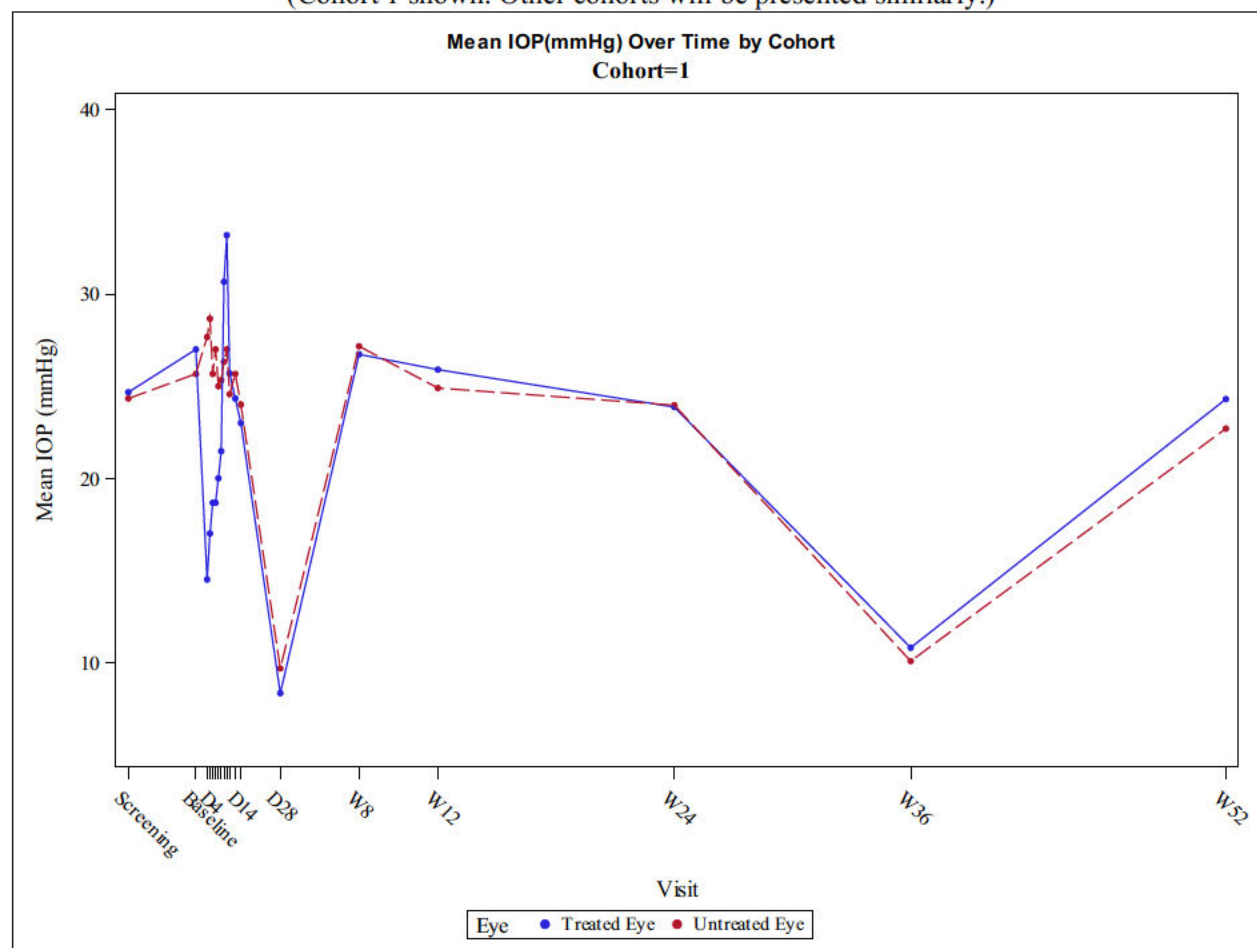


Figure 2. Mean IOP Over Time by Cohort

(Cohort 1 shown. Other cohorts will be presented similarly.)

**Figure 3. Mean Change in IOP from Baseline Over Time by Cohort**

This figure will be similar to Figure 2.

Figure 4. IOP Over Time by Subject

(One subject plot shown. Other subject plots will be presented similarly.)

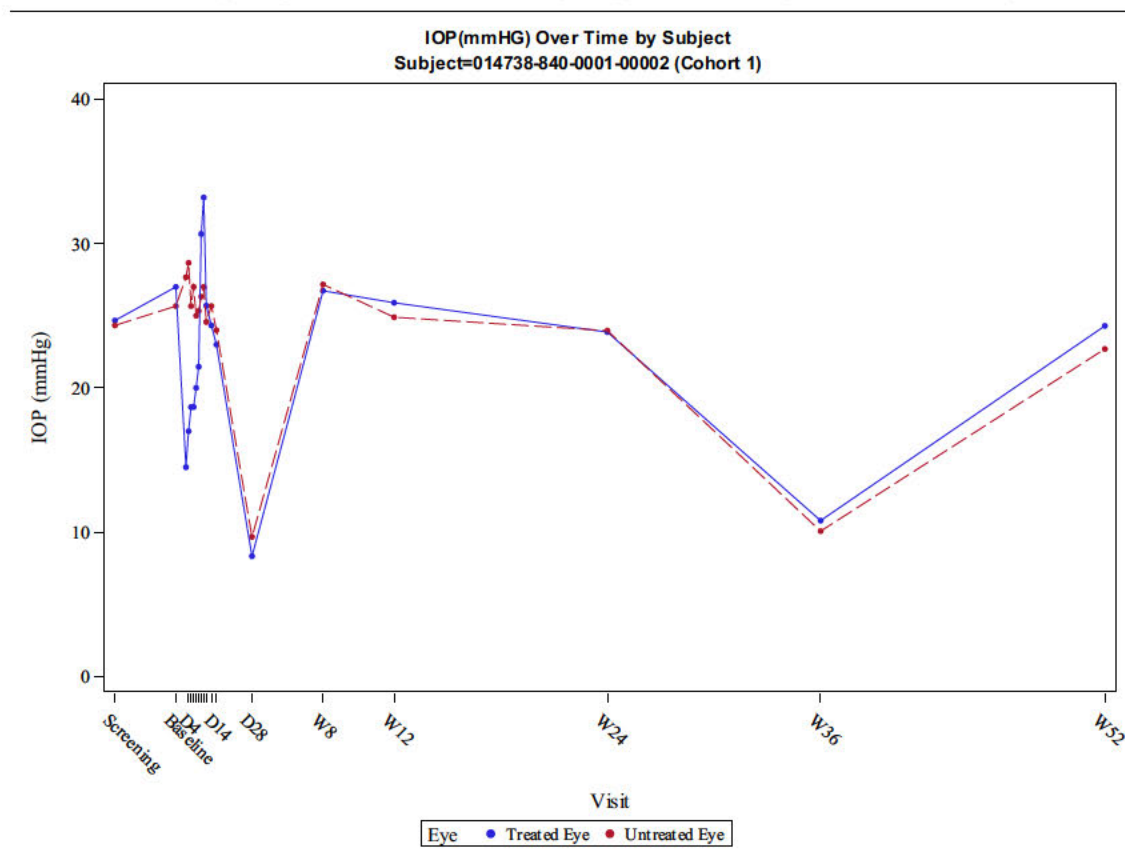


Figure 5. Change in IOP from Baseline Over Time by Subject

This figure will be similar to Figure 4.

Figure 6. Anti-AAV5 Titer Over Time by Cohort and Subject

(Cohort 1 shown. Other cohorts will be presented similarly.)

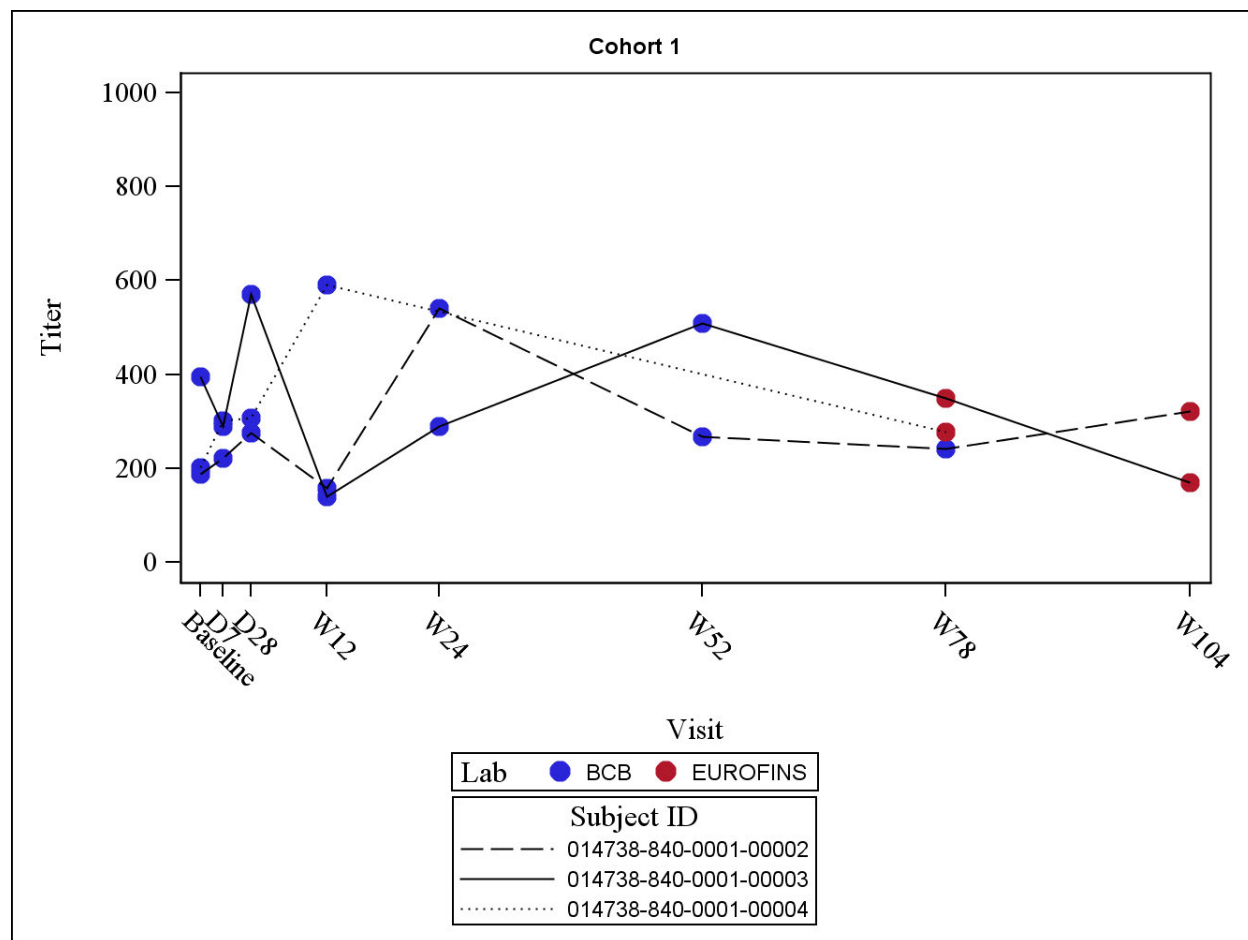


Figure 7. Anti-RetGC1 Titer Over Time by Cohort and Subject

This figure will be similar to Figure 6.

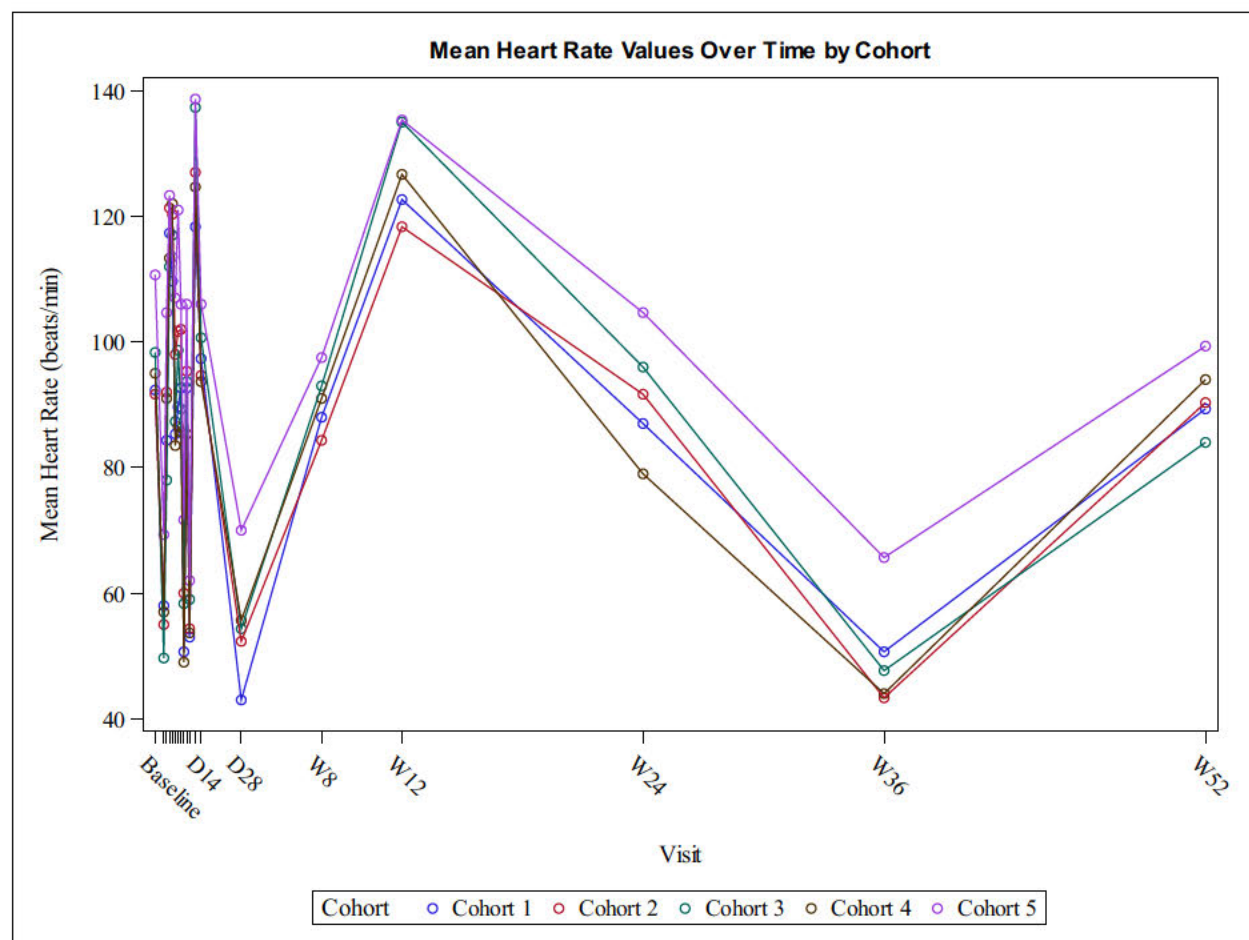
Figure 8. Mean Heart Rate Values Over Time by Cohort

Figure 9. Mean Systolic Blood Pressure Over Time by Cohort

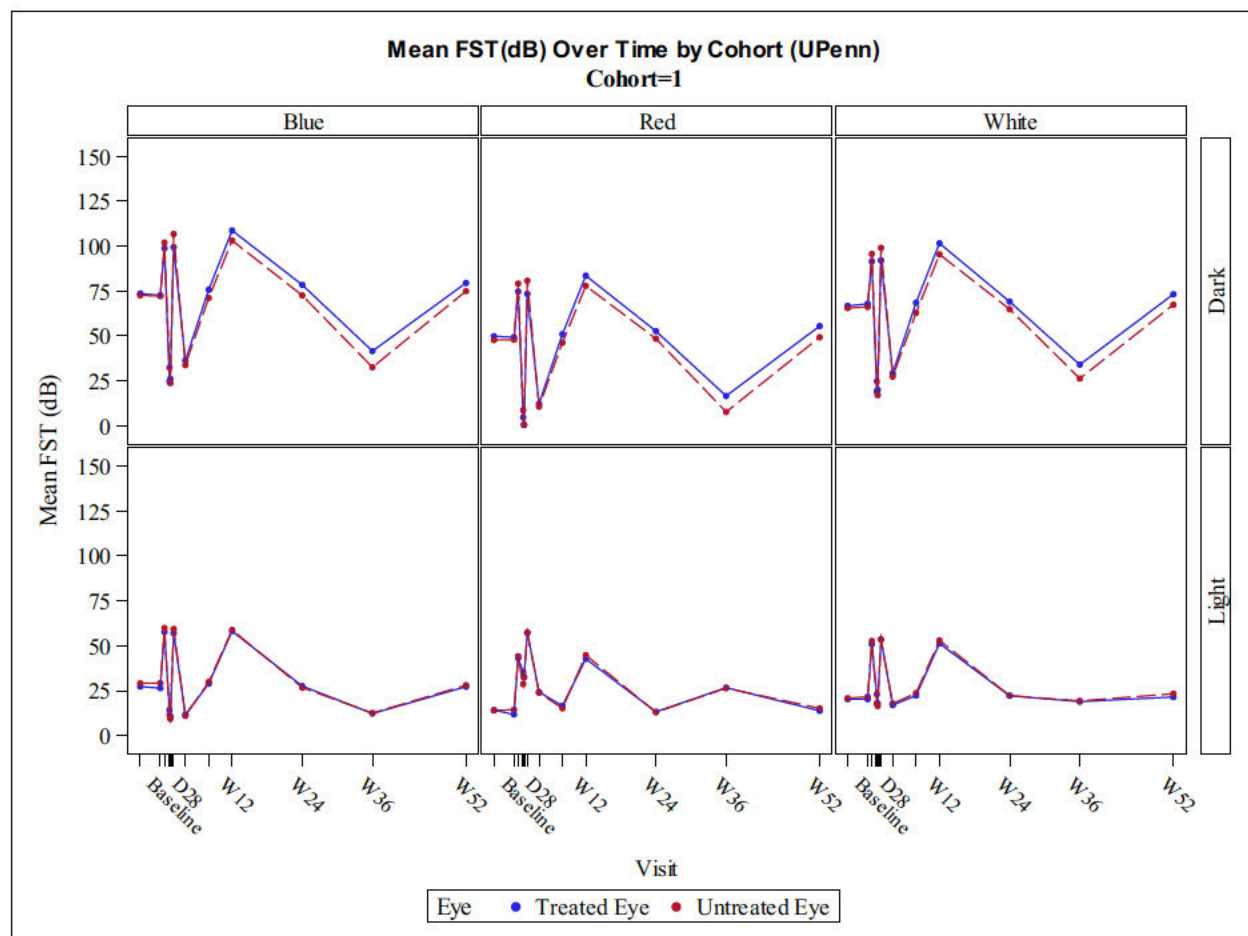
This figure will be similar to Figure 8.

Figure 10. Mean Diastolic Blood Pressure Over Time by Cohort

This figure will be similar to Figure 8.

Figure 11. Mean FST (decibels) Over Time by Cohort (UPenn)

(Cohort 1 shown. Other cohorts will be presented similarly.)

**Figure 12. Mean Change in FST (decibels) from Baseline Over Time by Cohort (All Sites)**

This figure will be similar to Figure 11.

Figure 13. Mean Change in Dark Adapted FST (decibels) from Baseline Over Time for High-Dose Cohorts (All Sites)

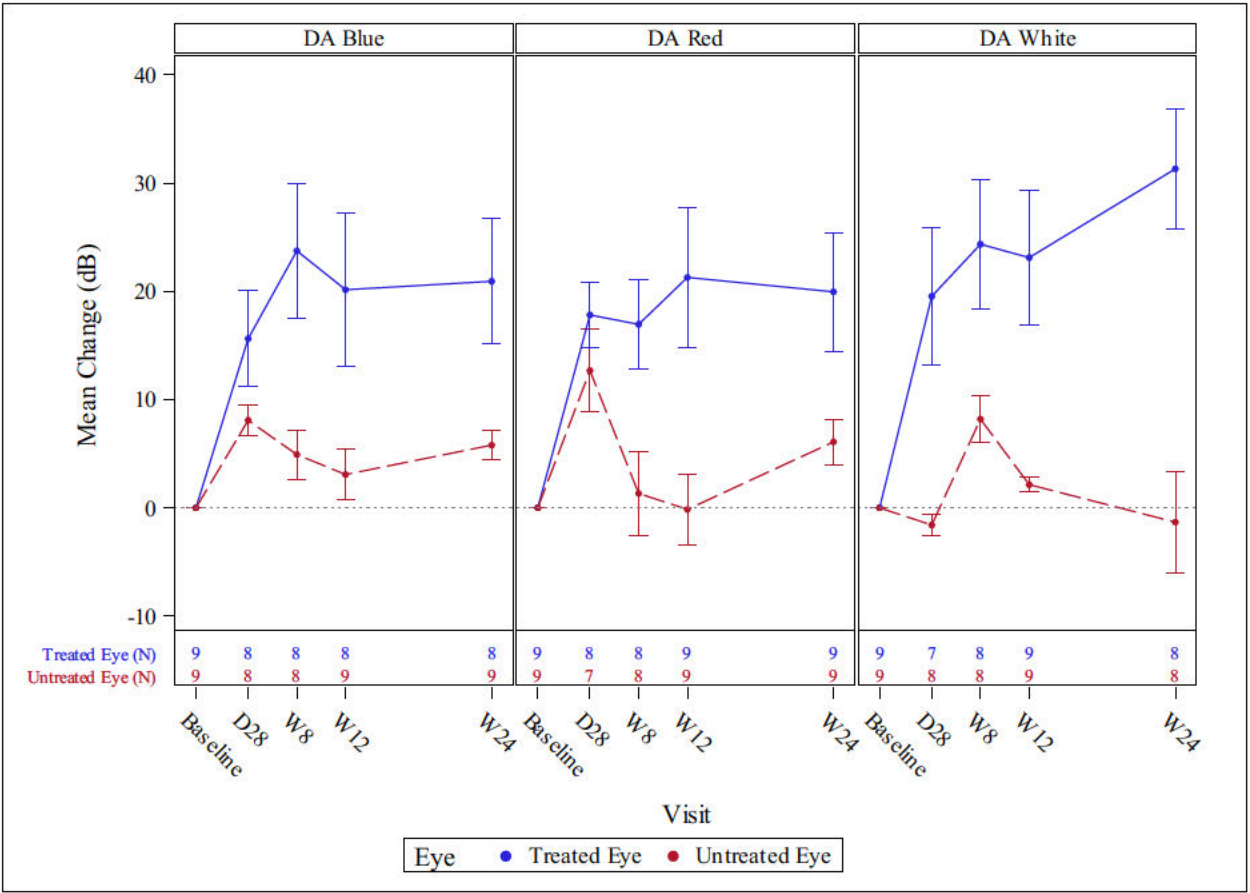


Figure 14. Mean Change in Treated Eye Dark Adapted FST (decibels) from Baseline Over Time for Cohort 1, Cohort 2, and High-Dose Cohorts (All Sites)

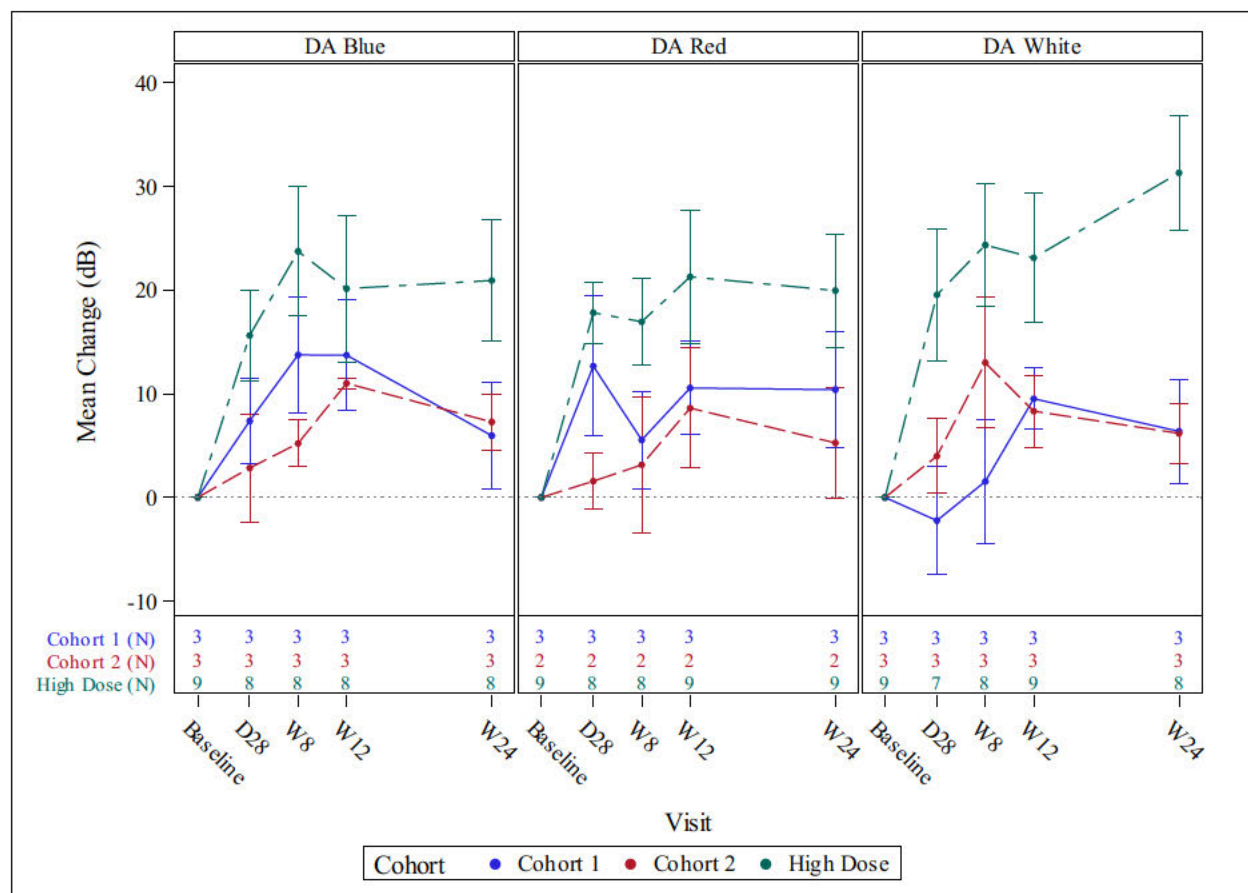


Figure 15. FST (decibels) Over Time by Subject (UPenn)

This figure will be similar to Figure 11.

Figure 16. FST (decibels) Over Time by Subject (OHSU)

This figure will be similar to Figure 11.

Figure 17. Change in FST (decibels) from Baseline Over Time by Subject (All Sites)

This figure will be similar to Figure 11.

Figure 18. Spaghetti Plot of FST (decibels) Over Time by Subject (UPenn)

This figure will be similar to Figure 11. All subjects from a cohort will be plotted together.

Figure 19. Spaghetti Plot of Change in FST (decibels) from Baseline Over Time by Subject (All Sites)

This figure will be similar to Figure 11. All subjects from a cohort will be plotted together.

Figure 20. Mean BCVA (logMAR) Over Time by Cohort

This figure will be similar to Figure 2.

Figure 21. Mean BCVA (ETDRS letters) Over Time by Cohort

This figure will be similar to Figure 2.

Figure 22. Mean Change in BCVA (logMAR) Over Time by Cohort

This figure will be similar to Figure 2.

Figure 23. Mean Change in BCVA (ETDRS letters) Over Time by Cohort

This figure will be similar to Figure 2.

Figure 24. Mean Change in BCVA (logMAR) from Baseline Over Time for Cohort 1, Cohort 2, and High-Dose Cohorts

This figure will be similar to Figure 13. The panels of the figures will be by cohort (Cohort 1, Cohort 2, and High-Dose).

Figure 25. BCVA (logMAR) Over Time by Subject

This figure will be similar to Figure 4.

Figure 26. BCVA (ETDRS letters) Over Time by Subject

This figure will be similar to Figure 4.

Figure 27. Change in BCVA (logMAR) from Baseline Over Time by Subject

This figure will be similar to Figure 4.

Figure 28. Change in BCVA (ETDRS letters) from Baseline Over Time by Subject

This figure will be similar to Figure 4.

Figure 29. Spaghetti Plot for BCVA (logMAR) Over Time by Subject

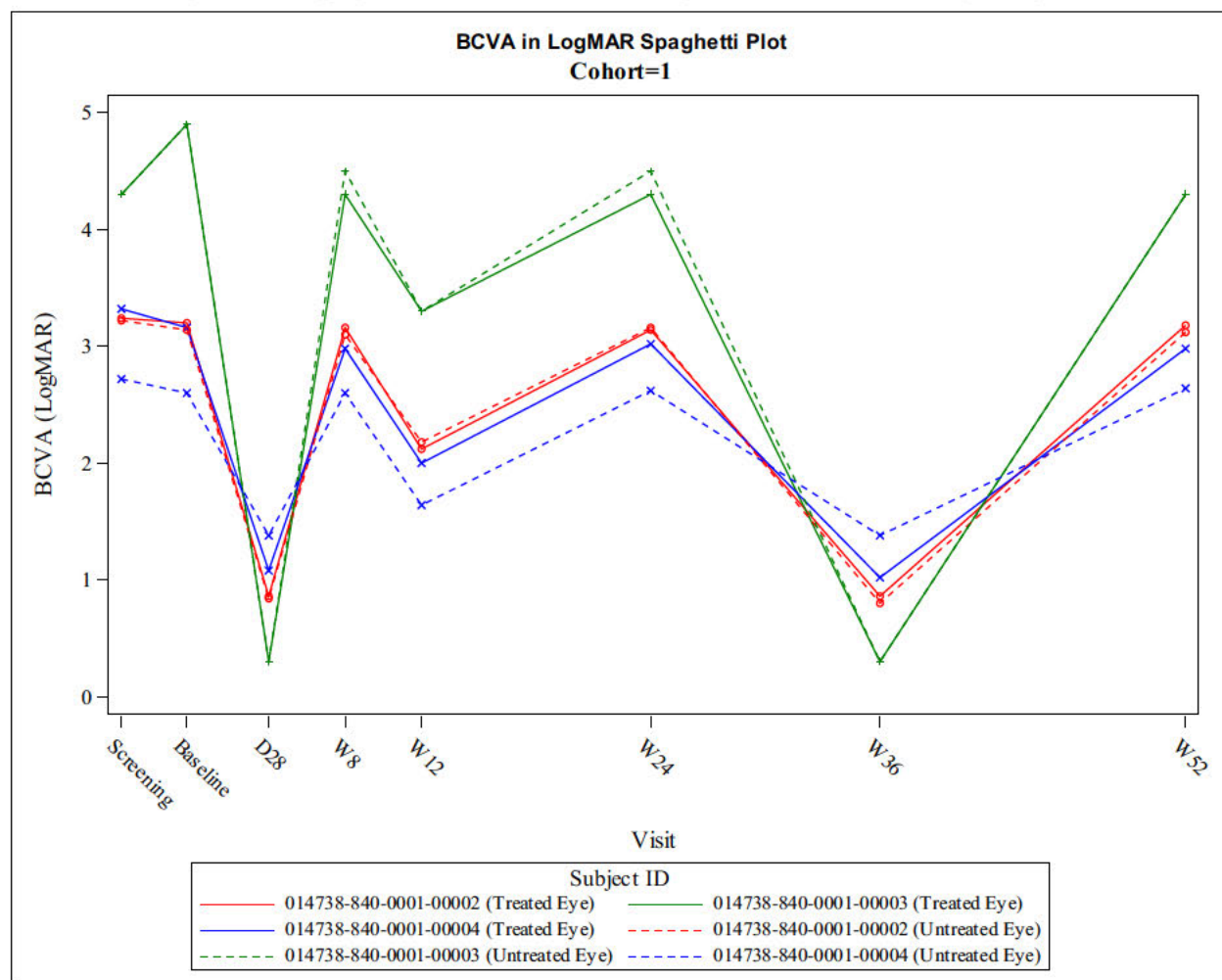


Figure 30. Spaghetti Plot for Change in BCVA (logMAR) from Baseline Over Time by Subject

This figure will be similar to Figure 29. Screening visit will be excluded.

Figure 31. Mean TPLR Response Threshold Over Time by Cohort (UPenn)

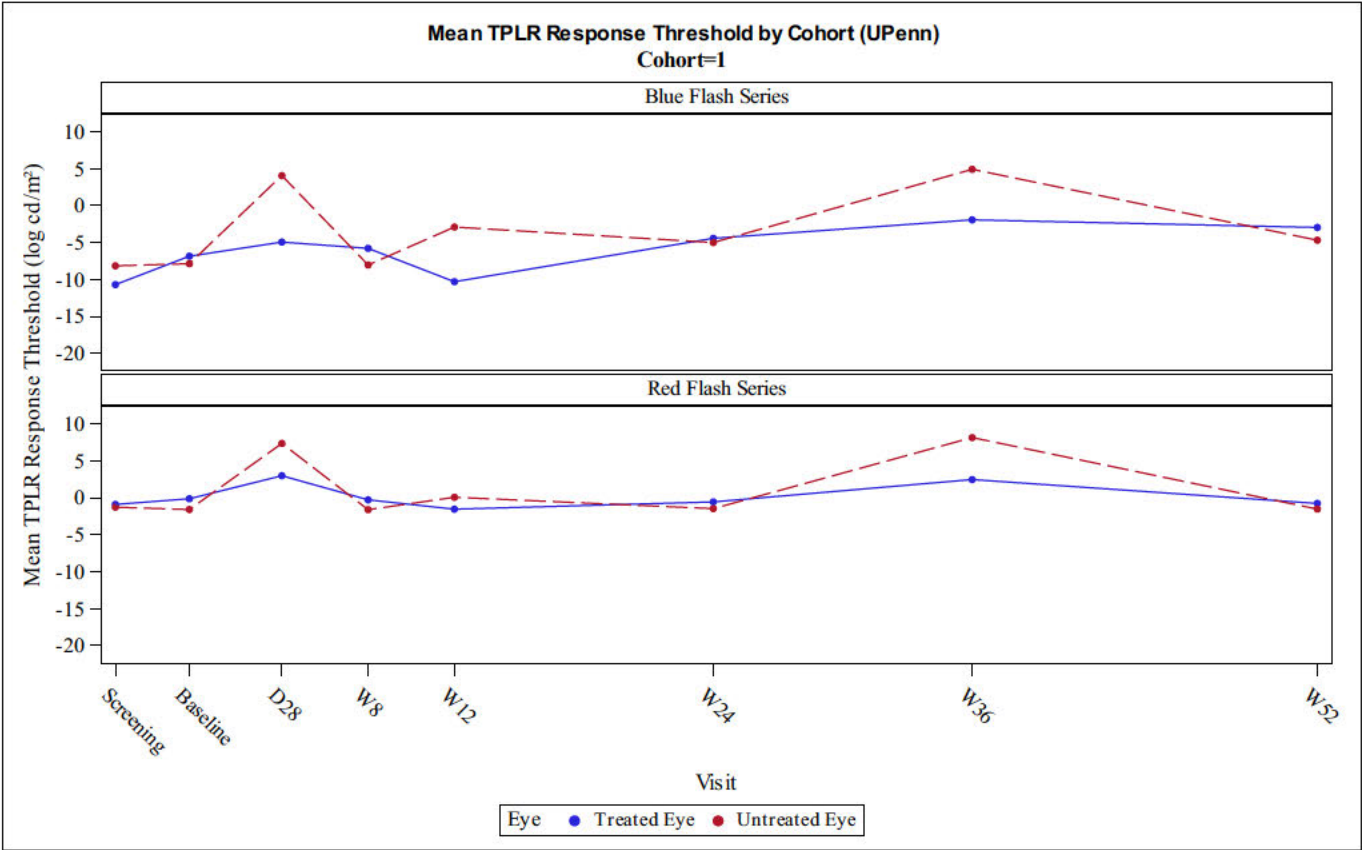


Figure 32. Mean Change in TPLR Response Threshold Over Time by Cohort (UPenn)

This figure will be similar to Figure 31.

Figure 33. Mean Retinal Thickness at the Fovea as Assessed by OCT Over Time by Cohort - EDC

This figure will be similar to Figure 2.

Figure 34. Mean Change in Retinal Thickness at the Fovea as Assessed by OCT from Baseline Over Time by Cohort - EDC

This figure will be similar to Figure 2.

Figure 35. Mean Change in EZ Line Width Within Central 5mm as Assessed by OCT from Baseline Over Time by Cohort - MERIT

This figure will be similar to Figure 31. Horizontal and vertical will be presented in the two rows.

Figure 36. Mean Change in Mean Retinal Thickness as Assessed by OCT from Baseline Over Time by Cohort - MERIT

This figure will be similar to Figure 31. Horizontal and vertical will be presented in the two rows.

Figure 37. Mean OCT Bleb Mean Retinal Thickness Over Time by Cohort - MERIT

This figure will be similar to Figure 2.

Figure 38. Mean Change in NEI VFQ-25 Composite Score from Baseline Over Time by Cohort

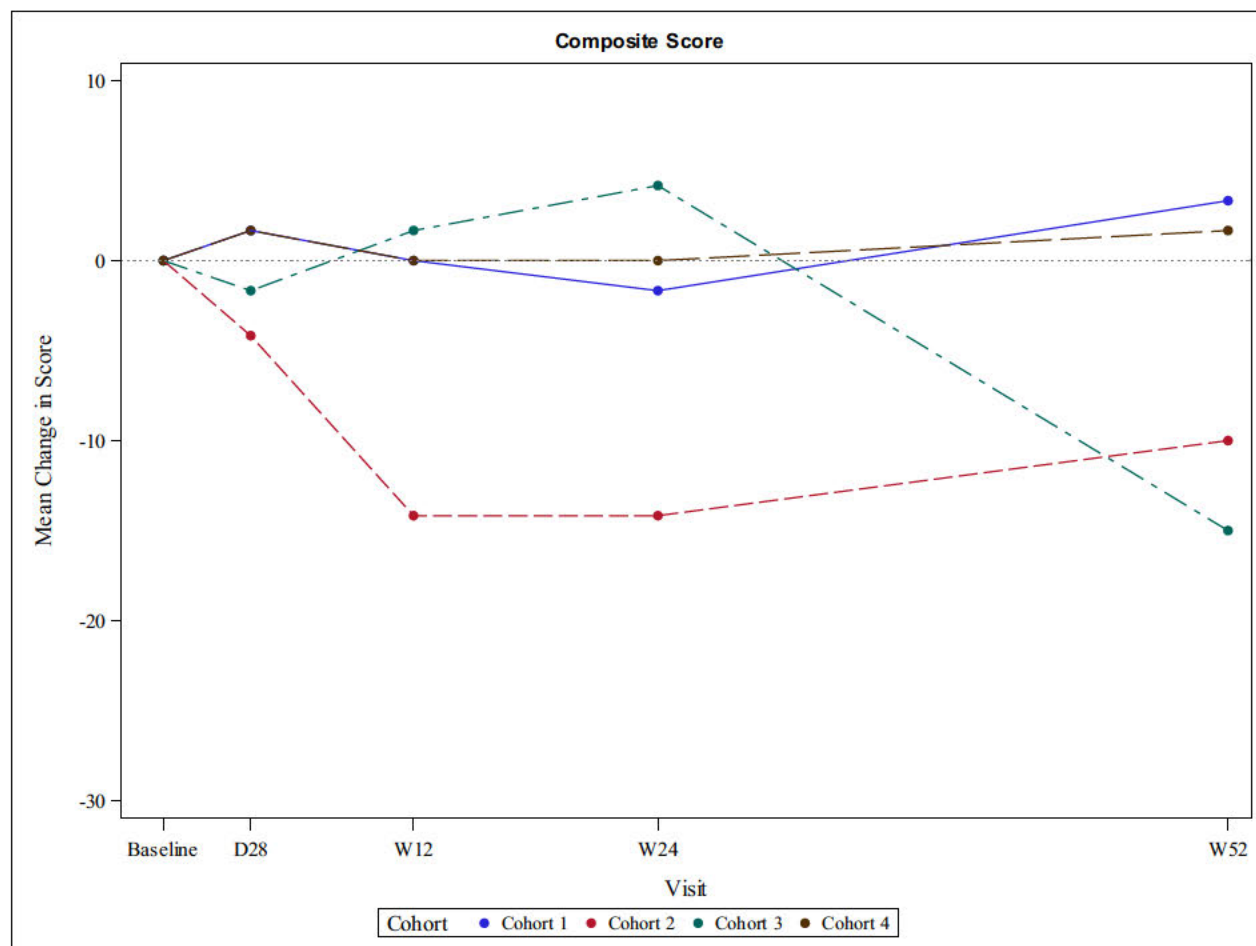


Figure 39. Mean Change in CVAQC Composite Score from Baseline Over Time for Cohort 5

This figure will be similar to Figure 38. Only one line will be plotted for Cohort 5.

Figure 40. Mobility Testing Scores Over Time by Subject (UPenn)

This figure will be similar to Figure 4.

Figure 41. Change in Mobility Testing Scores Over Time by Subject (UPenn)

This figure will be similar to Figure 4.

APPENDIX 4. LISTINGS**LIST OF LISTINGS**

Listing 1. Subject Terminations.....	101
Listing 2. Subject Demographics.....	102
Listing 3. Medical History	102
Listing 4. ATSN-101 Treatment Exposure and Compliance.....	103
Listing 5. Medications Prior to ATSN-101 Administration	103
Listing 6. Concomitant Medications.....	104
Listing 7. NIMP Treatment.....	104
Listing 8. Major Protocol Deviations.....	104
Listing 9. Protocol Deviations	104
Listing 10. Treatment-emergent Adverse Events	105
Listing 11. TEAEs Leading to Death.....	106
Listing 12. Serious TEAEs	106
Listing 13. TEAEs Leading to Treatment Discontinuation	106
Listing 14. Adverse Events of Special Interest.....	106
Listing 15. Results of Ocular Examinations (Slit Lamp Examination and Ophthalmoscopy).....	106
Listing 16. Intraocular Pressure	107
Listing 17. Fundus Photography	107
Listing 18. Subjects Having Laboratory PCSA	108
Listing 19. Subjects with Laboratory Parameters Outside of Normal Range.....	108
Listing 20. Hematology Values	109
Listing 21. Chemistry Values	109
Listing 22. Urinalysis Values.....	110
Listing 23. ADA AAV5 and RetGC1 Results	110
Listing 24. ELISpot to AAV5 Results	111
Listing 25. ELISpot to RetGC1 Results.....	111
Listing 26. Subjects with Treatment-Emergent Positive ADA to AAV5	112
Listing 27. Subjects with Treatment-Emergent Positive ADA to RetGC1	112
Listing 28. Subjects with Treatment-Emergent Positive ELISpot to AAV5	112

Listing 29. Subjects with Treatment-Emergent Positive ELISpot to RetGC1.....	112
Listing 30. AESIs and SAEs for Subjects with Positive ADA to AAV5 Result at Baseline.....	113
Listing 31. AESIs and SAEs for Subjects with Positive ADA to RetGC1 Result at Baseline.....	113
Listing 32. AESIs and SAEs for Subjects with Detected ELISpot to AAV5 Result at Baseline.....	113
Listing 33. AESIs and SAEs for Subjects with Detected ELISpot to RetGC1 Result at Baseline.....	113
Listing 34. AESIs and SAEs for Subjects with Treatment-Emergent Positive ADA to AAV5 Result	113
Listing 35. AESIs and SAEs for Subjects with Treatment-Emergent Positive ADA to RetGC1 Result	114
Listing 36. AESIs and SAEs for Subjects with Treatment-Emergent Positive ELISpot to AAV5 Result	114
Listing 37. AESIs and SAEs for Subjects with Treatment-Emergent Positive ELISpot to RetGC1 Result	114
Listing 38. Vital Signs	114
Listing 39. Subjects Having Vital Signs PCSA	115
Listing 40. Subjects with Vital Signs Outside of Normal Range	115
Listing 41. Full-field Stimulus Testing – Decibels (UPenn)	116
Listing 42. Full-field Stimulus Testing – Decibels (OHSU)	116
Listing 43. Full-field Stimulus Testing – Log Units (UPenn)	117
Listing 44. Full-field Stimulus Testing – Log Units (OHSU)	117
Listing 45. Best-corrected Visual Acuity - logMAR	118
Listing 46. Best-corrected Visual Acuity – ETDRS letters	118
Listing 47. Pupillometry – EDC	118
Listing 48. TPLR Amplitude (UPenn).....	119
Listing 49. TPLR Response Threshold (UPenn)	119
Listing 50. Pupillometry – MERIT (OHSU)	120
Listing 51. Oculomotor Instability.....	120
Listing 52. Photoaversion	121
Listing 53. Low-luminance Visual Acuity (OHSU).....	121
Listing 54. Optical Coherence Tomography – EDC.....	122

Listing 55. Optical Coherence Tomography – MERIT	122
Listing 56. Bleb Optical Coherence Tomography – MERIT	122
Listing 57. NEI Visual Function Questionnaire-25 Results	123
Listing 58. Cardiff Visual Ability Questionnaire for Children Results	123
Listing 59. Patient’s Experience Due to Changes in Vision (PECV) Questionnaire.....	123
Listing 60. Mobility Testing Results (UPenn).....	124

Listing 1. Subject Terminations

Cohort	Subject ID	Received Treatment	Days from Surgery ^a	Termination Reason	Specify	Date of Last Available Information
1	XX	XX	XX	XX	XX	XX
	XX	XX	XX	XX	XX	XX
..	XX	XX	XX	XX	XX	XX
5	XX	XX	XX	XX	XX	XX
	XX	XX	XX	XX	XX	XX

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

^a Days from surgery at time of termination.

Listing 2. Subject Demographics

Cohort	Subject ID	Age (years)	Gender	Race	Ethnicity	Height (cm)	Weight (kg)	BMI (kg/m ²)	Allele 1	Allele 2
1	xx	xx	xx	xx	xx	xx	xx.x	xx.x	xx	xx
	xx	xx	xx	xx	xx	xx	xx.x	xx.x	xx	xx
...	xx	xx	xx	xx	xx	xx	xx.x	xx.x	xx	xx
5	xx	xx	xx	xx	xx	xx	xx.x	xx.x	xx	xx
	xx	xx	xx	xx	xx	xx	xx.x	xx.x	xx	xx

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

Listing 3. Medical History

Cohort	Subject ID	A/G/R ^a	Surgery Date	Medical History Term	MedDRA SOC ^b	MedDRA PT ^b	Start Date	End Date
1	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
5	xx	xx/xx/xx	xx	xx	xx	xx	xx	xx
	xx	xx/xx/xx	xx	xx	xx	xx	xx	xx

Abbreviations: SOC = System Organ Class, PT = Preferred Term

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Age (years) / Gender (M=Male, F=Female) / Race (W=White, B=Black or African American, A=Asian, AI=American Indian or Alaska Native, PI=Native Hawaiian or Other Pacific Islander, NR= Not Reported, UN=Unknown)

^b MedDRA Version XX.X

Listing 4. ATSN-101 Treatment Exposure and Compliance

Cohort	Subject ID	A/G/R ^a	Surgery Date	Treated Eye	Vector Genomes Per Eye	Volume (μL)	Was Full Dose (300μL) Administered?	If No, Specify
1	XX	x/x/x	XX	XX	XX	XX	XX	XX
...	XX	x/x/x	XX	XX	XX	XX	XX	XX
	XX	x/x/x	XX	XX	XX	XX	XX	XX
5	XX	x/x/x	XX	XX	XX	XX	XX	XX
	XX	x/x/x	XX	XX	XX	XX	XX	XX

^a Age (years) / Gender (M=Male, F=Female) / Race (W=White, B=Black or African American, A=Asian, AI=American Indian or Alaska Native, PI=Native Hawaiian or Other Pacific Islander, NR= Not Reported, UN=Unknown)

Listing 5. Medications Prior to ATSN-101 Administration

Cohort	Subject ID	A/G/R ^a	Surgery Date	Medication	Start Date	Duration ^b	Daily Dose	Route	Reason
XX	XX	x/x/x	XX	XX	XX	XX	XX	XX	XX
XX	XX	x/x/x	XX	XX	XX	XX	XX	XX	XX
...	XX	x/x/x	XX	XX	XX	XX	XX	XX	XX

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Age (years) / Gender (M=Male, F=Female) / Race (W=White, B=Black or African American, A=Asian, AI=American Indian or Alaska Native, PI=Native Hawaiian or Other Pacific Islander, NR= Not Reported, UN=Unknown)

^b Duration is the total number of days from medication start date to medication end date + 1. If medication start date is missing a day, then the day is imputed to the first of the month. If the medication end date is missing a day, then the day is imputed to be the last day of the month. If the medication start date is missing a month and day, then the month and day are imputed to January 1. If the medication end date is missing a month and a day, then the month and day are imputed to be December 31.

* indicates duration calculated with imputed medication start and/or end date.

Listing 6. Concomitant Medications

This listing will be similar to Listing 5.

Listing 7. NIMP Treatment

This listing will be similar to Listing 5.

Listing 8. Major Protocol Deviations

Cohort	Subject ID	Visit	Study Day	Category	Term	Coded Term	Description
XX	XX	XX	XX	XX	XX	XX	XX
XX	XX	XX	XX	XX	XX	XX	XX
...	XX	XX	XX	XX	XX	XX	XX

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

Listing 9. Protocol Deviations

This listing will be similar to Listing 8.

Listing 10. Treatment-emergent Adverse Events

Cohort	Subject ID	Start Date	Duration^a	Reported Term	MedDRA PT^b	Outcome	Effect on IMP	Effect on NIMP	Related to IMP	Related to NIMP	Related to Study Procedures	Related to Surgical Procedure	Severity	SAE	AESI
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

Abbreviations: PT = Preferred Term, IMP = Investigational Medicinal Product, NIMP = Non-investigational Medicinal Product, SAE = Serious Adverse Event, AESI = Adverse Event of Special Interest

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Duration is the total number of days from the event date to resolution date + 1. If event start date is missing a day, then the day is imputed to the first of the month. If the event end date is missing a day, then the day is imputed to be the last day of the month. If the event start date is missing a month and day, then the month and day are imputed to January 1. If the event end date is missing a month and a day, then the month and day are imputed to be December 31. * indicates duration calculated with imputed event start and/or end date.

^b MedDRA Version: XX.X

Listing 11. TEAEs Leading to Death

This listing will be similar to Listing 10. The columns for Severity and SAE will be excluded.

Listing 12. Serious TEAEs

This listing will be similar to Listing 10. The column for SAE will be excluded.

Listing 13. TEAEs Leading to Treatment Discontinuation

This listing will be similar to Listing 10.

Listing 14. Adverse Events of Special Interest

This listing will be similar to Listing 10. The column for AESI will be excluded.

Listing 15. Results of Ocular Examinations (Slit Lamp Examination and Ophthalmoscopy)

Cohort	Subject ID	Visit	Study Day	Method of Examination	Location	Name of Examination	Treated Eye		Untreated Eye	
							Result	If Abnormal, Clinically Significant?	Result	If Abnormal, Clinically Significant?
1	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
5	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

Listing 16. Intraocular Pressure

Cohort	Subject ID	Visit	Study Day	Method of Examination	Treated Eye		Untreated Eye	
					Result (mmHg)	Δ (mmHg)	Result (mmHg)	Δ (mmHg)
1	XX	XX	XX	XX	XX.X	XX.X	XX.X	XX.X
...	XX	XX	XX	XX	XX.X	XX.X	XX.X	XX.X
5	XX	XX	XX	XX	XX.X	XX.X	XX.X	XX.X
...	XX	XX	XX	XX	XX.X	XX.X	XX.X	XX.X

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

Δ indicates change from baseline.

Listing 17. Fundus Photography

Cohort	Subject ID	Visit	Study Day	Change from Baseline?	Change Considered Clinically Significant?
1	XX	XX	XX	XX	XX
...	XX	XX	XX	XX	XX
5	XX	XX	XX	XX	XX
...	XX	XX	XX	XX	XX

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

Listing 18. Subjects Having Laboratory PCSA

Cohort	Subject ID	A/G/R ^a	Visit	Study Day	Parameter Category	Laboratory Parameter (Units)	Value (Flag) ^b
XX	XX	x/x/x	XX	XX	XX	XX	XX
XX	XX	x/x/x	XX	XX	XX	XX	XX
...	XX	x/x/x	XX	XX	XX	XX	XX

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

^a Age (years) / Gender (M=Male, F=Female) / Race (W=White, B=Black or African American, A=Asian, AI=American Indian or Alaska Native, PI=Native Hawaiian or Other Pacific Islander, NR= Not Reported, UN=Unknown).

^b Flags – SCR: Screening; B: baseline; Pre: pre-treatment; T: treatment emergent; - or +: value reaching the lower or upper PCSA limit.

Listing 19. Subjects with Laboratory Parameters Outside of Normal Range

Cohort	Subject ID	A/G/R ^a	Visit	Study Day	Parameter Category	Laboratory Parameter (Units)	Value	Reference Range Indicator
XX	XX	x/x/x	XX	XX	XX	XX	XX	XX
XX	XX	x/x/x	XX	XX	XX	XX	XX	XX
...	XX	x/x/x	XX	XX	XX	XX	XX	XX

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

^a Age (years) / Gender (M=Male, F=Female) / Race (W=White, B=Black or African American, A=Asian, AI=American Indian or Alaska Native, PI=Native Hawaiian or Other Pacific Islander, NR= Not Reported, UN=Unknown).

Listing 20. Hematology Values

Cohort	Subject ID	A/G/R ^a	Visit	Study Day	Laboratory Parameter (Units)	Result	Reference Range	Reference Range Indicator
1	xx	x/x/x	xx	xx	xx	xx.xx	xx.xx – xx.xx	xx
...	xx	x/x/x	xx	xx	xx	xx.xx	xx.xx – xx.xx	xx
	xx	x/x/x	xx	xx	xx	xx.xx	xx.xx – xx.xx	xx
5	xx	x/x/x	xx	xx	xx	xx.xx	xx.xx – xx.xx	xx
...	xx	x/x/x	xx	xx	xx	xx.xx	xx.xx – xx.xx	xx

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Age (years) / Gender (M=Male, F=Female) / Race (W=White, B=Black or African American, A=Asian, AI=American Indian or Alaska Native, PI=Native Hawaiian or Other Pacific Islander, NR= Not Reported, UN=Unknown).

Listing 21. Chemistry Values

Cohort	Subject ID	A/G/R ^a	Visit	Study Day	Fasting Status	Laboratory Parameter (Units)	Result	Reference Range	Reference Range Indicator
1	xx	x/x/x	xx	xx	xx	xx	xx.xx	xx.xx – xx.xx	xx
...	xx	x/x/x	xx	xx	xx	xx	xx.xx	xx.xx – xx.xx	xx
	xx	x/x/x	xx	xx	xx	xx	xx.xx	xx.xx – xx.xx	xx
5	xx	x/x/x	xx	xx	xx	xx	xx.xx	xx.xx – xx.xx	xx
...	xx	x/x/x	xx	xx	xx	xx	xx.xx	xx.xx – xx.xx	xx

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Age (years) / Gender (M=Male, F=Female) / Race (W=White, B=Black or African American, A=Asian, AI=American Indian or Alaska Native, PI=Native Hawaiian or Other Pacific Islander, NR= Not Reported, UN=Unknown)

Listing 22. Urinalysis Values

Cohort	Subject ID	A/G/R ^a	Visit	Study Day	Laboratory Parameter	Result
1	xx	xx/xx/xx	xx	xx	xx	xx
			xx	xx	xx	xx
...	xx	xx/xx/xx	xx	xx	xx	xx
			xx	xx	xx	xx
5	xx	xx/xx/xx	xx	xx	xx	xx
...	xx	xx/xx/xx	xx	xx	xx	xx

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

^a Age (years) / Gender (M=Male, F=Female) / Race (W=White, B=Black or African American, A=Asian, AI=American Indian or Alaska Native, PI=Native Hawaiian or Other Pacific Islander, NR= Not Reported, UN=Unknown)

Listing 23. ADA AAV5 and RetGC1 Results

Cohort	Subject ID	A/G/R ^a	Visit	Study Day	Anti AAV5 Screen	Anti AAV5 Confirm	Anti AAV5 Titer	Anti RetGC1 Screen	Anti RetGC1 Confirm	Anti RetGC1 Titer
1	xx	x/x/x	xx	xx	xx	xx	xx	xx	xx	xx
...	xx	x/x/x	xx	xx	xx	xx	xx	xx	xx	xx
	xx	x/x/x	xx	xx	xx	xx	xx	xx	xx	xx
5	xx	x/x/x	xx	xx	xx	xx	xx	xx	xx	xx
...	xx	x/x/x	xx	xx	xx	xx	xx	xx	xx	xx

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

^a Age (years) / Gender (M=Male, F=Female) / Race (W=White, B=Black or African American, A=Asian, AI=American Indian or Alaska Native, PI=Native Hawaiian or Other Pacific Islander, NR= Not Reported, UN=Unknown)

Listing 24. ELISpot to AAV5 Results

Cohort	Subject ID	A/G/R ^a	Visit	Study Day	Immunology Test	AAV5 Pool 1	AAV5 Pool 2	AAV5 Pool 3
1	xx	x/x/x	xx	xx	xx	xx	xx	xx
...	xx	x/x/x	xx	xx	xx	xx	xx	xx
5	xx	x/x/x	xx	xx	xx	xx	xx	xx
...	xx	x/x/x	xx	xx	xx	xx	xx	xx

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

^a Age (years) / Gender (M=Male, F=Female) / Race (W=White, B=Black or African American, A=Asian, AI=American Indian or Alaska Native, PI=Native Hawaiian or Other Pacific Islander, NR= Not Reported, UN=Unknown)

Listing 25. ELISpot to RetGC1 Results

Cohort	Subject ID	A/G/R ^a	Visit	Study Day	Immunology Test	RetGC1 Pool 1	RetGC1 Pool 2	RetGC1 Pool 3	RetGC1 Pool 4	RetGC1 Pool 5
1	xx	x/x/x	xx	xx	xx	xx	xx	xx	xx	xx
...	xx	x/x/x	xx	xx	xx	xx	xx	xx	xx	xx
5	xx	x/x/x	xx	xx	xx	xx	xx	xx	xx	xx
...	xx	x/x/x	xx	xx	xx	xx	xx	xx	xx	xx

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

^a Age (years) / Gender (M=Male, F=Female) / Race (W=White, B=Black or African American, A=Asian, AI=American Indian or Alaska Native, PI=Native Hawaiian or Other Pacific Islander, NR= Not Reported, UN=Unknown)

Listing 26. Subjects with Treatment-Emergent Positive ADA to AAV5

Cohort	Subject ID	A/G/R ^a	Visit	Study Day
xx	xx	x/x/x	xx	xx
...	xx	x/x/x	xx	xx
	xx	x/x/x	xx	xx
xx	xx	x/x/x	xx	xx
...	xx	x/x/x	xx	Xx

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

Treatment-emergent positivity is defined as: 1) a post-baseline result that is positive when the baseline result is negative or 2) a post-baseline result that has a titer greater than or equal to 4 times the baseline titer when the baseline result is positive, while titer values are available at both baseline and post-baseline visits.

^a Age (years) / Gender (M=Male, F=Female) / Race (W=White, B=Black or African American, A=Asian, AI=American Indian or Alaska Native, PI=Native Hawaiian or Other Pacific Islander, NR= Not Reported, UN=Unknown)

Listing 27. Subjects with Treatment-Emergent Positive ADA to RetGC1

This listing will be similar to Listing 26.

Listing 28. Subjects with Treatment-Emergent Positive ELISpot to AAV5

This listing will be similar to Listing 26.

Listing 29. Subjects with Treatment-Emergent Positive ELISpot to RetGC1

This listing will be similar to Listing 26.

Listing 30. AESIs and SAEs for Subjects with Positive ADA to AAV5 Result at Baseline

Cohort	Subject ID	Start Date	Duration ^a	Reported Term	MedDRA PT ^b	Outcome	Effect on IMP	Effect on NIMP	Related to IMP	Related to NIMP	Related to Study Procedures	Related to Surgical Procedure	Severity	SAE	AESI
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

Abbreviations: PT = Preferred Term, IMP = Investigational Medicinal Product, NIMP = Non-investigational Medicinal Product

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Duration is the total number of days from the event date to resolution date + 1.

^b MedDRA Version: XX.X

Listing 31. AESIs and SAEs for Subjects with Positive ADA to RetGC1 Result at Baseline

This listing will be similar to Listing 30.

Listing 32. AESIs and SAEs for Subjects with Detected ELISpot to AAV5 Result at Baseline

This listing will be similar to Listing 30.

Listing 33. AESIs and SAEs for Subjects with Detected ELISpot to RetGC1 Result at Baseline

This listing will be similar to Listing 30.

Listing 34. AESIs and SAEs for Subjects with Treatment-Emergent Positive ADA to AAV5 Result

This listing will be similar to Listing 30.

Listing 35. AESIs and SAEs for Subjects with Treatment-Emergent Positive ADA to RetGC1 Result

This listing will be similar to Listing 30.

Listing 36. AESIs and SAEs for Subjects with Treatment-Emergent Positive ELISpot to AAV5 Result

This listing will be similar to Listing 30.

Listing 37. AESIs and SAEs for Subjects with Treatment-Emergent Positive ELISpot to RetGC1 Result

This listing will be similar to Listing 30.

Listing 38. Vital Signs

Cohort	Subject ID	A/G/R ^a	Visit	Study Day	Diastolic Blood Pressure (mmHg)	Systolic Blood Pressure (mmHg)	Heart Rate (beats/min)	Temperature (C)
1	xx	x/x/x	xx	xx	xx	xx	xx	xx.x
...	xx	x/x/x	xx	xx	xx	xx	xx	xx.x
	xx	x/x/x	xx	xx	xx	xx	xx	xx.x
5	xx	x/x/x	xx	xx	xx	xx	xx	xx.x
...	xx	x/x/x	xx	xx	xx	xx	xx	xx.x

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

^a Age (years) / Gender (M=Male, F=Female) / Race (W=White, B=Black or African American, A=Asian, AI=American Indian or Alaska Native, PI=Native Hawaiian or Other Pacific Islander, NR= Not Reported, UN=Unknown)

Listing 39. Subjects Having Vital Signs PCSA

Cohort	Subject ID	A/G/R ^a	Visit	Study Day	Parameter (Units)	Value (Flag) ^b
xx	xx	x/x/x	xx	xx	xx	xx
xx	xx	x/x/x	xx	xx	xx	xx
...	xx	x/x/x	xx	xx	xx	xx

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

^a Age (years) / Gender (M=Male, F=Female) / Race (W=White, B=Black or African American, A=Asian, AI=American Indian or Alaska Native, PI=Native Hawaiian or Other Pacific Islander, NR= Not Reported, UN=Unknown).

^b Flags – B: baseline; Pre: pre-treatment; T: treatment emergent; - or +: value reaching the lower or upper PCSA limit.

Listing 40. Subjects with Vital Signs Outside of Normal Range

Cohort	Subject ID	A/G/R ^a	Visit	Study Day	Parameter (Units)	Value
xx	xx	x/x/x	xx	xx	xx	xx
xx	xx	x/x/x	xx	xx	xx	xx
...	xx	x/x/x	xx	xx	xx	xx

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

^a Age (years) / Gender (M=Male, F=Female) / Race (W=White, B=Black or African American, A=Asian, AI=American Indian or Alaska Native, PI=Native Hawaiian or Other Pacific Islander, NR= Not Reported, UN=Unknown).

Listing 41. Full-field Stimulus Testing – Decibels (UPenn)

Cohort	Subject ID	Visit	Study Day	Condition	Stimulus	Treated Eye			Untreated Eye		
						EDC Result ^a (dB)	Analysis Result ^b (dB)	Δ^c (dB)	EDC Result ^a (dB)	Analysis Result ^b (dB)	Δ^c (dB)
1	xx	xx	xx	xx	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
...					...	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
					...	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
5	xx	xx	xx	xx	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
...					...	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
					...	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

^a Result reported in EDC.

^b Result used for analysis.

^c Δ indicates change from baseline from analysis result.

Listing 42. Full-field Stimulus Testing – Decibels (OHSU)

This listing will be similar to Listing 41.

Listing 43. Full-field Stimulus Testing – Log Units (UPenn)

Cohort	Subject ID	Visit	Study Day	Dark Adaptation Time (Both Eyes) (min)	Light Adapting Field Intensity (Both Eyes) (cd/m ²)	Condition	Stimulus	Treated Eye		Untreated Eye	
								Result (log units)	Δ (log units)	Result (log units)	Δ (log units)
1	xx	xx	xx	xx	xx	xx	xx	xx.x	xx.x	xx.x	xx.x
...							...	xx.x	xx.x	xx.x	xx.x
							...	xx.x	xx.x	xx.x	xx.x
5	xx	xx	xx	xx	xx	xx	xx	xx.x	xx.x	xx.x	xx.x
...							...	xx.x	xx.x	xx.x	xx.x
							...	xx.x	xx.x	xx.x	xx.x

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

Δ indicates change from baseline.

Listing 44. Full-field Stimulus Testing – Log Units (OHSU)

This listing will be similar to Listing 43.

Listing 45. Best-corrected Visual Acuity - logMAR

Cohort	Subject ID	Visit	Study Day	Method of Examination	Name of Examination	Correction	Treated Eye (logMAR)		Untreated Eye (logMAR)	
							Result	Δ	Result	Δ
1	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
5	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

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

Δ indicates change from baseline.

Listing 46. Best-corrected Visual Acuity – ETDRS letters

This listing will be similar to Listing 45. Columns for Method of Examination, Name of Examination, and Correction will be excluded.

Listing 47. Pupillometry – EDC

Cohort	Subject ID	Visit	Study Day	Series	Method of Examination	Log Luminance (cd/m ²)	Treated Eye		Untreated Eye	
							Result (mm)	Δ (mm)	Result (mm)	Δ (mm)
1	xx	xx	xx	xx	xx	xx	xx.x	xx.x	xx.x	xx.x
...				xx	xx	xx	xx.x	xx.x	xx.x	xx.x
5	xx	xx	xx	xx	xx	xx	xx.x	xx.x	xx.x	xx.x
...				xx	xx	xx	xx.x	xx.x	xx.x	xx.x

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

Δ indicates change from baseline.

Listing 48. TPLR Amplitude (UPenn)

Cohort	Subject ID	Visit	Study Day	Series	Log Luminance (cd/m ²)	Treated Eye		Untreated Eye	
						Result (mm)	Δ (mm)	Result (mm)	Δ (mm)
1	xx	xx	xx	xx	xx	xx.x	xx.x	xx.x	xx.x
...				xx	xx	xx.x	xx.x	xx.x	xx.x
5	xx	xx	xx	xx	xx	xx.x	xx.x	xx.x	xx.x
...				xx	xx	xx.x	xx.x	xx.x	xx.x

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

Δ indicates change from baseline.

Listing 49. TPLR Response Threshold (UPenn)

Cohort	Subject ID	Visit	Study Day	Series	Treated Eye		Untreated Eye	
					Result (log cd/m ²)	Δ (log cd/m ²)	Result (log cd/m ²)	Δ (log cd/m ²)
1	xx	xx	xx	xx	xx.xx	xx.xx	xx.xx	xx.xx
...				xx	xx.xx	xx.xx	xx.xx	xx.xx
5	xx	xx	xx	xx	xx.xx	xx.xx	xx.xx	xx.xx
...				xx	xx.xx	xx.xx	xx.xx	xx.xx

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

Δ indicates change from baseline.

Listing 50. Pupillometry – MERIT (OHSU)

Cohort	Subject ID	Visit	Study Day	Examination (Units)	Treated Eye		Untreated Eye	
					Result	Δ	Result	Δ
4	xx	xx	xx	xx	x.xx	x.xx	x.xx	x.xx
				xx	x.xx	x.xx	x.xx	x.xx
5	xx	xx	xx					
...								

Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

Δ indicates change from baseline.

Listing 51. Oculomotor Instability

Cohort	Subject ID	Visit	Study Day	Name of Examination	Fixation	Treated Eye		Untreated Eye	
						Result (mm)	Δ (mm)	Result (mm)	Δ (mm)
1	xx	xx	xx	xx	xx	xx.xx	xx.xx	xx.xx	xx.xx
...					xx	xx.xx	xx.xx	xx.xx	xx.xx
5	xx	xx	xx	xx	xx	xx.xx	xx.xx	xx.xx	xx.xx
...					xx	xx.xx	xx.xx	xx.xx	xx.xx

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

Δ indicates change from baseline.

Listing 52. Photoaversion

Cohort	Subject ID	Visit	Study Day	Treated Eye		Untreated Eye	
				Result (cd/m ²)	Δ (cd/m ²)	Result (cd/m ²)	Δ (cd/m ²)
1	XX	XX	XX	XX.X	XX.X	XX.X	XX.X
...	XX	XX	XX	XX.X	XX.X	XX.X	XX.X
5	XX	XX	XX	XX.X	XX.X	XX.X	XX.X
...	XX	XX	XX	XX.X	XX.X	XX.X	XX.X

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

Δ indicates change from baseline.

Listing 53. Low-luminance Visual Acuity (OHSU)

Cohort	Subject ID	Visit	Study Day	Treated Eye		Untreated Eye	
				Result (letters read)	Δ (letters read)	Result (letters read)	Δ (letters read)
1	XX	XX	XX	XX.X	XX.X	XX.X	XX.X
...	XX	XX	XX	XX.X	XX.X	XX.X	XX.X
5	XX	XX	XX	XX.X	XX.X	XX.X	XX.X
...	XX	XX	XX	XX.X	XX.X	XX.X	XX.X

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

Δ indicates change from baseline.

Listing 54. Optical Coherence Tomography – EDC

Cohort	Subject ID	Visit	Study Day	Sub-location in Eye	Name of Examination	Treated Eye			Untreated Eye		
						Result	If Abnormal, Reason	Δ	Result	If Abnormal, Reason	Δ
1	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
...	xx	xx	xx	xx	xx	xx.x	xx	xx.x	xx.x	xx	xx.x
5	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
...	xx	xx	xx	xx	xx	xx.x	xx	xx.x	xx.x	xx	xx.x

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

Δ indicates change from baseline.

Listing 55. Optical Coherence Tomography – MERIT

Cohort	Subject ID	Visit	Study Day	Name of Examination	Treated Eye		Untreated Eye	
					Result	Δ	Result	Δ
1	xx	xx	xx	xx	xx	xx	xx	xx
...	xx	xx	xx	xx	xx.x	xx.x	xx.x	xx.x
5	xx	xx	xx	xx	xx	xx	xx	xx
...	xx	xx	xx	xx	xx.x	xx.x	xx.x	xx.x

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

Δ indicates change from baseline.

Listing 56. Bleb Optical Coherence Tomography – MERIT

This listing will be similar to Listing 55.

Listing 57. NEI Visual Function Questionnaire-25 Results

Cohort	Subject ID	A/G/R ^a	Visit	Study Day	Subcategory for Question	Question Name	Response
1	xx	xx/xx/xx	xx	xx	xx	xx	xx
...	xx	xx/xx/xx	xx	xx	xx	xx	xx
5	xx	xx/xx/xx	xx	xx	xx	xx	xx
	xx	xx/xx/xx	xx	xx	xx	xx	xx

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye.

^a Age (years) / Gender (M=Male, F=Female) / Race (W=White, B=Black or African American, A=Asian, AI=American Indian or Alaska Native, PI=Native Hawaiian or Other Pacific Islander, NR= Not Reported, UN=Unknown)

Listing 58. Cardiff Visual Ability Questionnaire for Children Results

This listing will be similar to Listing 57.

Listing 59. Patient's Experience Due to Changes in Vision (PECV) Questionnaire

Cohort	Subject ID	A/G/R ^a	Visit	Study Day	Changes in Vision Since Start of Study?	Specify Changes
1	xx	xx/xx/xx	xx	xx	xx	xx
...	xx	xx/xx/xx	xx	xx	xx	xx
5	xx	xx/xx/xx	xx	xx	xx	xx
	xx	xx/xx/xx	xx	xx	xx	xx

Cohort 1 is 1.0x10¹⁰ vg/eye. Cohort 2 is 3.0x10¹⁰ vg/eye. Cohort 3 is 1.0x10¹¹ vg/eye. Cohort 4 is 1.0x10¹¹ vg/eye. Cohort 5 is 1.0x10¹¹ vg/eye.

^a Age (years) / Gender (M=Male, F=Female) / Race (W=White, B=Black or African American, A=Asian, AI=American Indian or Alaska Native, PI=Native Hawaiian or Other Pacific Islander, NR= Not Reported, UN=Unknown).

Listing 60. Mobility Testing Results (UPenn)

Cohort	Subject ID	A/G/R^a	Eye	Light Level (lux)^b	Visit #/Day # Result	Visit #/Day # Result	Visit #/Day # Result	...
1	xx	xx/xx/xx	Treated Eye	1	Pass/Fail	Pass/Fail	Pass/Fail	
				4	Pass/Fail	Pass/Fail	Pass/Fail	
				10	Pass/Fail	Pass/Fail	Pass/Fail	
				...	Pass/Fail	Pass/Fail	Pass/Fail	
				Score	xx	xx	xx	
5	xx	xx/xx/xx	Untreated Eye	1	Pass/Fail	Pass/Fail	Pass/Fail	
				...	Pass/Fail	Pass/Fail	Pass/Fail	
					Pass/Fail	Pass/Fail	Pass/Fail	
...					Pass/Fail	Pass/Fail	Pass/Fail	
...					Pass/Fail	Pass/Fail	Pass/Fail	

Cohort 1 is 1.0×10^{10} vg/eye. Cohort 2 is 3.0×10^{10} vg/eye. Cohort 3 is 1.0×10^{11} vg/eye. Cohort 4 is 1.0×10^{11} vg/eye. Cohort 5 is 1.0×10^{11} vg/eye.

^a Age (years) / Gender (M=Male, F=Female) / Race (W=White, B=Black or African American, A=Asian, AI=American Indian or Alaska Native, PI=Native Hawaiian or Other Pacific Islander, NR= Not Reported, UN=Unknown)

^b Score corresponds to MLMT score code for lowest level with the first “Pass” result.

APPENDIX 5. ICH E3 NUMBERING

ICH E3 Section	ICH E3 TFL Number	TFL Title	SAP TFL No.
14.1	Table 14.1.1	Subject Disposition by Cohort	Table 1
	Table 14.1.2	Summary of Protocol Deviations by Cohort	Table 6
	Table 14.1.3	Summary of Demographics by Cohort	Table 2
	Table 14.1.4	Summary of Medical History by Cohort	Table 3
	Table 14.1.5	Summary of Concomitant Medications by WHO Drug Classification and Cohort	Table 5
	Table 14.1.6	Summary of Treatment Exposure and Compliance by Cohort	Table 4
	Figure 14.1.1	Consort Diagram	Figure 1
14.2 - Secondary Efficacy - FST	Table 14.2.2.1.1.1	FST (decibels) Analysis Results - Dark Adapted	Table 57
	Table 14.2.2.1.1.2	FST (decibels) Analysis Results - Light Adapted	Table 58
	Table 14.2.2.1.2.1	Summary of Changes in FST (decibels) Over Time by Cohort – Red, Light Adapted (All Sites)	Table 45
	Table 14.2.2.1.2.2	Summary of Changes in FST (decibels) Over Time by Cohort – Red, Dark Adapted (All Sites)	Table 46
	Table 14.2.2.1.2.3	Summary of Changes in FST (decibels) Over Time by Cohort – White, Light Adapted (All Sites)	Table 47
	Table 14.2.2.1.2.4	Summary of Changes in FST (decibels) Over Time by Cohort – White, Dark Adapted (All Sites)	Table 48
	Table 14.2.2.1.2.5	Summary of Changes in FST (decibels) Over Time by Cohort – Blue, Light Adapted (All Sites)	Table 49
	Table 14.2.2.1.2.6	Summary of Changes in FST (decibels) Over Time by Cohort – Blue, Dark Adapted (All Sites)	Table 50
	Table 14.2.2.1.3.1	Summary of Difference in Change from Baseline in FST (decibels) Between the Treated and Untreated Eyes Over Time by Cohort – Red, Light Adapted (All Sites)	Table 51

	Table 14.2.2.1.3.2	Summary of Difference in Change from Baseline in FST (decibels) Between the Treated and Untreated Eyes Over Time by Cohort – Red, Dark Adapted (All Sites)	Table 52
	Table 14.2.2.1.3.3	Summary of Difference in Change from Baseline in FST (decibels) Between the Treated and Untreated Eyes Over Time by Cohort – White, Light Adapted (All Sites)	Table 53
	Table 14.2.2.1.3.4	Summary of Difference in Change from Baseline in FST (decibels) Between the Treated and Untreated Eyes Over Time by Cohort – White, Dark Adapted (All Sites)	Table 54
	Table 14.2.2.1.3.5	Summary of Difference in Change from Baseline in FST (decibels) Between the Treated and Untreated Eyes Over Time by Cohort – Blue, Light Adapted (All Sites)	Table 55
	Table 14.2.2.1.3.6	Summary of Difference in Change from Baseline in FST (decibels) Between the Treated and Untreated Eyes Over Time by Cohort – Blue, Dark Adapted (All Sites)	Table 56
	Figure 14.2.2.1.1	Mean FST (decibels) Over Time by Cohort (UPenn)	Figure 11
	Figure 14.2.2.1.2	Mean Change in FST (decibels) from Baseline Over Time by Cohort (All Sites)	Figure 12
	Figure 14.2.2.1.4	Mean Change in Dark Adapted FST (decibels) from Baseline Over Time for High-Dose Cohorts (All Sites)	Figure 13
	Figure 14.2.2.1.5	Mean Change in Treated Eye Dark Adapted FST (decibels) from Baseline Over Time for Cohort 1, Cohort 2, and High-Dose Cohorts (All Sites)	Figure 14
	Figure 14.2.2.1.6.1	FST (decibels) Over Time by Subject (UPenn)	Figure 15
	Figure 14.2.2.1.6.2	FST (decibels) Over Time by Subject (OHSU)	Figure 16
	Figure 14.2.2.1.6.3	Spaghetti Plot of FST (decibels) Over Time by Subject (UPenn)	Figure 18
	Figure 14.2.2.1.7.1	Change in FST (decibels) from Baseline Over Time by Subject (All Sites)	Figure 17
	Figure 14.2.2.1.7.2	Spaghetti Plot of Change in FST (decibels) from Baseline Over Time by Subject (All Sites)	Figure 19
14.2 - Secondary Efficacy - BCVA	Table 14.2.2.2.1.1	BCVA (logMAR) Analysis Results	Table 65
	Table 14.2.2.2.1.2	BCVA (ETDRS letters) Analysis Results	Table 66
	Table 14.2.2.2.2.1	Summary of BCVA (logMAR) Over Time by Cohort	Table 59

	Table 14.2.2.2.2.2	Summary of BCVA (ETDRS letters) Over Time by Cohort	Table 60
	Table 14.2.2.2.3.1	Summary of Changes in BCVA (logMAR) from Baseline Over Time by Cohort	Table 61
	Table 14.2.2.2.3.2	Summary of Changes in BCVA (ETDRS letters) from Baseline Over Time by Cohort	Table 62
	Table 14.2.2.2.4.1	Summary of Difference in BCVA (logMAR) Between the Treated and Untreated Eyes Over Time by Cohort	Table 63
	Table 14.2.2.2.4.2	Summary of Difference in BCVA (ETDRS letters) Between the Treated and Untreated Eyes Over Time by Cohort	Table 64
	Figure 14.2.2.2.2.1	Mean BCVA (logMAR) Over Time by Cohort	Figure 20
	Figure 14.2.2.2.2.2	Mean BCVA (ETDRS letters) Over Time by Cohort	Figure 21
	Figure 14.2.2.2.3.1	Mean Change in BCVA (logMAR) Over Time by Cohort	Figure 22
	Figure 14.2.2.2.3.2	Mean Change in BCVA (ETDRS letters) Over Time by Cohort	Figure 23
	Figure 14.2.2.2.3.3	Mean Change in BCVA (logMAR) from Baseline Over Time for Cohort 1, Cohort 2, and High-Dose Cohorts	Figure 24
	Figure 14.2.2.2.5.1	BCVA (logMAR) Over Time by Subject	Figure 25
	Figure 14.2.2.2.5.2	BCVA (ETDRS letters) Over Time by Subject	Figure 26
	Figure 14.2.2.2.5.3	Spaghetti Plot for BCVA (logMAR) Over Time by Subject	Figure 29
	Figure 14.2.2.2.6.1	Change in BCVA (logMAR) from Baseline Over Time by Subject	Figure 27
	Figure 14.2.2.2.6.2	Change in BCVA (ETDRS letters) from Baseline Over Time by Subject	Figure 28
	Figure 14.2.2.2.6.3	Spaghetti Plot for Change in BCVA (logMAR) from Baseline Over Time by Subject	Figure 30
14.2 - Exploratory Efficacy - Pupillometry	Table 14.2.3.1.2.1	Summary of Changes in TPLR Response Threshold from Baseline Over Time by Cohort – Red (UPenn)	Table 67
	Table 14.2.3.1.2.2	Summary of Changes in TPLR Response Threshold from Baseline Over Time by Cohort – Blue (UPenn)	Table 68
	Figure 14.2.3.1.1	Mean TPLR Response Threshold Over Time by Cohort (UPenn)	Figure 31
	Figure 14.2.3.1.2	Mean Change in TPLR Response Threshold Over Time by Cohort (UPenn)	Figure 32

14.2 - Exploratory Efficacy - Oculomotor Instability	Table 14.2.3.2.1.1	Summary of Changes in Overall OCI from Baseline Over Time by Cohort – Fixation Off	Table 69
	Table 14.2.3.2.1.2	Summary of Changes in Overall OCI from Baseline Over Time by Cohort – Fixation On	Table 70
14.2 - Exploratory Efficacy - Photoaversion	Table 14.2.3.3.1	Summary of Changes in Photoaversion Threshold Over Time by Cohort	Table 71
14.2 - Exploratory Efficacy - LLVA	NA (listing only)		
14.2 - Exploratory Efficacy - OCT	Table 14.2.3.5.2	Summary of Changes in Retinal Thickness at the Fovea as Assessed by OCT from Baseline Over Time by Cohort – EDC	Table 72
	Table 14.2.3.5.3.1	Summary of Changes in Mean Retinal Thickness as Assessed by OCT (Horizontal) from Baseline Over Time by Cohort – MERIT	Table 76
	Table 14.2.3.5.3.2	Summary of Changes in Mean Retinal Thickness as Assessed by OCT (Vertical) from Baseline Over Time by Cohort – MERIT	Table 77
	Table 14.2.3.5.4	Summary of Changes in OCT Bleb Mean Retinal Thickness from Baseline Over Time by Cohort – MERIT	Table 79
	Table 14.2.3.5.5	Summary of Changes in EZ Line Extending +/- 5 Degrees from Fovea as Assessed by OCT from Baseline Over Time by Cohort – EDC	Table 73
	Table 14.2.3.5.6.1	Summary of Changes in EZ Line Width Within Central 5mm as Assessed by OCT (Horizontal) from Baseline Over Time by Cohort – MERIT	Table 74
	Table 14.2.3.5.6.2	Summary of Changes in EZ Line Width Within Central 5mm as Assessed by OCT (Vertical) from Baseline Over Time by Cohort – MERIT	Table 75
	Table 14.2.3.5.7	Summary of Changes in Foveal EZ Line as Assessed by OCT from Baseline Over Time by Cohort – MERIT	Table 78
	Figure 14.2.3.5.1	Mean Retinal Thickness at Fovea as Assessed by OCT Over Time by Cohort – EDC	Figure 33
	Figure 14.2.3.5.2	Mean Change in Retinal Thickness at Fovea as Assessed by OCT from Baseline Over Time by Cohort – EDC	Figure 34
	Figure 14.2.3.5.3	Mean Change in Mean Retinal Thickness as Assessed by OCT from Baseline Over Time by Cohort – MERIT	Figure 36

	Figure 14.2.3.5.4	Mean OCT Bleb Mean Retinal Thickness Over Time by Cohort – MERIT	Figure 37
	Figure 14.2.3.5.6	Mean Change in EZ Line Width Within Central 5mm as Assessed by OCT from Baseline Over Time by Cohort – MERIT	Figure 35
14.2 - Exploratory Efficacy - Visual Function Questionnaire	Table 14.2.3.6.1	Summary of Changes in NEI VFQ-25 Composite and Sub-scale Scores from Baseline Over Time by Cohort (Cohorts 1-4)	Table 80
	Table 14.2.3.6.2	Summary of Changes in CVAQC Composite and Subscale Scores from Baseline Over Time for Cohort 5	Table 81
	Figure 14.2.3.6.1	Mean Change in NEI VFQ-25 Composite Score from Baseline Over Time by Cohort	Figure 38
	Figure 14.2.3.6.2	Mean Change in CVAQC Composite Score from Baseline Over Time for Cohort 5	Figure 39
14.2 - Exploratory Efficacy - PECV Questionnaire	Table 14.2.3.7.1	Summary of PECV Questionnaire Over Time by Cohort	Table 82
14.2 - Exploratory Efficacy - Mobility Testing	Figure 14.2.3.8.1	Mobility Testing Scores Over Time by Subject (UPenn)	Figure 40
	Figure 14.2.3.8.2	Change in Mobility Testing Scores Over Time by Subject (UPenn)	Figure 41
14.3.1 - Displays of AEs	Table 14.3.1.1	Overview of TEAEs by Cohort	Table 7
	Table 14.3.1.2	Summary of TEAEs by System Organ Class, Preferred Term, Severity, and Cohort	Table 8
	Table 14.3.1.3	Summary of Adverse Events by Follow-up Period and Cohort	Table 42
	Table 14.3.1.4	Summary of TEAEs Related to IMP by System Organ Class, Preferred Term, Severity, and Cohort	Table 9
	Table 14.3.1.5	Summary of TEAEs Related to NIMP by System Organ Class, Preferred Term, Severity and Cohort	Table 10
	Table 14.3.1.6	Summary of TEAEs Related to Study Procedures by System Organ Class, Preferred Term, Severity, and Cohort	Table 11
	Table 14.3.1.7	Summary of TEAEs Related to Surgical Procedure by System Organ Class, Preferred Term, Severity, and Cohort	Table 12
14.3.2 - Listings of Deaths, Other Serious and Significant AEs	Table 14.3.2.1.1	Overview of Serious TEAEs by Cohort	Table 13
	Table 14.3.2.1.2	Summary of Serious TEAEs by System Organ Class, Preferred Term, Severity, and Cohort	Table 14
	Table 14.3.2.1.3	Summary of Serious TEAEs Related to Surgical Procedure by System Organ Class, Preferred Term, Severity, and Cohort	Table 15

	Table 14.3.2.1.4	Summary of Serious Adverse Events by Follow-up Period and Cohort	Table 43
	Table 14.3.2.1.5	Summary of SAEs by Baseline ADA Assay Result	Table 31
	Table 14.3.2.1.6	Summary of SAEs by Baseline ELISpot Assay Result	Table 33
	Table 14.3.2.1.7	Summary of SAEs by Treatment-emergent ADA Assay	Table 35
	Table 14.3.2.1.8	Summary of SAEs by Treatment-emergent ELISpot Assay	Table 37
	Table 14.3.2.2.1	Summary of AESIs by AESI Category, Preferred Term, and Cohort	Table 16
	Table 14.3.2.2.2	Summary of AESIs by Follow-up Period and Cohort	Table 44
	Table 14.3.2.2.3	Summary of AESIs by Baseline ADA Assay Result	Table 30
	Table 14.3.2.2.4	Summary of AESIs by Baseline ELISpot Assay Result	Table 32
	Table 14.3.2.2.5	Summary of AESIs by Treatment-emergent ADA Assay	Table 34
	Table 14.3.2.2.6	Summary of AESIs by Treatment-emergent ELISpot Assay	Table 36
14.3.3 - Safety Narratives	NA		
14.3.4 - Abnormal Laboratory Value Listing	Table 14.3.4.1	Summary of Subjects with Post-Treatment Hematology Laboratory Parameters Outside of Normal Range by Cohort	Table 23
	Table 14.3.4.2	Summary of Subjects with Post-Treatment Chemistry Parameters Outside of Normal Range by Cohort	Table 24
	Table 14.3.4.3	Summary of Subjects with Post-baseline PCSAs in Laboratory Parameters by Cohort	Table 22
	Table 14.3.4.4	Summary of Heart Rate Over Time by Cohort	Table 38
	Table 14.3.4.5	Summary of Systolic Blood Pressure Over Time by Cohort	Table 39
	Table 14.3.4.6	Summary of Diastolic Blood Pressure Over Time by Cohort	Table 40
	Table 14.3.4.7	Summary of Subjects with PCSAs in Vital Signs by Cohort	Table 41
	Table 14.3.4.8	Summary of ADA AAV5 and RetGC1 Results Over Time by Cohort	Table 25
	Table 14.3.4.9	Summary of ELISpot to AAV5 Results Over Time by Cohort	Table 26
	Table 14.3.4.10	Summary of ELISpot to RetGC1 Results Over Time by Cohort	Table 27
	Table 14.3.4.11	Summary of Treatment-Emergent ADA Positivity Over Time by Cohort	Table 28
	Table 14.3.4.12	Summary of Treatment-Emergent ELISpot Positivity Over Time by Cohort	Table 29
	Figure 14.3.4.4	Mean Heart Rate Values Over Time by Cohort	Figure 8
	Figure 14.3.4.5	Mean Systolic Blood Pressure Over Time by Cohort	Figure 9

	Figure 14.3.4.6	Mean Diastolic Blood Pressure Over Time by Cohort	Figure 10
	Figure 14.3.4.7	Anti-AAV5 Titer Over Time by Cohort and Subject	Figure 6
	Figure 14.3.4.8	Anti-RetGC1 Titer Over Time by Cohort and Subject	Figure 7
14.3.5 - Ophthalmological Safety Data Summary Tables and Figures Note: 14.3.5 is not an ICH header, but can be added for organization	Table 14.3.5.1	Summary of Slit Lamp Assessments Over Time by Cohort – Anterior Chamber	Table 17
	Table 14.3.5.2.1	Summary of Ophthalmoscopy Assessments Over Time by Cohort – Macula	Table 18
	Table 14.3.5.2.2	Summary of Ophthalmoscopy Assessments Over Time by Cohort – Vitreous	Table 19
	Table 14.3.5.3	Summary of IOP (mmHg) Over Time by Cohort	Table 20
	Table 14.3.5.4	Summary of Changes in IOP (mmHg) from Baseline Over Time by Cohort	Table 21
	Figure 14.3.5.3	Mean IOP Over Time by Cohort	Figure 2
	Figure 14.3.5.4	Mean Change in IOP from Baseline Over Time by Cohort	Figure 3
	Figure 14.3.5.5	IOP Over Time by Subject	Figure 4
	Figure 14.3.5.6	Change in IOP from Baseline Over Time by Subject	Figure 5
16.2.1 - Discontinued Subjects	Listing 16.2.1.1	Subject Terminations	Listing 1
16.2.2 - Protocol Deviations	Listing 16.2.2.1	Protocol Deviations	Listing 9
	Listing 16.2.2.2	Major Protocol Deviations	Listing 8
16.2.3 - Subjects Excluded from Efficacy Analysis	NA		
16.2.4 - Demographic Data	Listing 16.2.4.1	Subject Demographics	Listing 2
	Listing 16.2.4.2	Medical History	Listing 3
	Listing 16.2.4.3	Medications Prior to ATSN-101 Administration	Listing 5
	Listing 16.2.4.4	Concomitant Medications	Listing 6
16.2.5 - Compliance and Drug Concentration Data	Listing 16.2.5.1	ATSN-101 Treatment Exposure and Compliance	Listing 4
	Listing 16.2.5.2	NIMP Treatment	Listing 7
16.2.6 - Individual Efficacy Response Data	Listing 16.2.6.1.1	Full-field Stimulus Testing – Decibels (UPenn)	Listing 41
	Listing 16.2.6.1.2	Full-field Stimulus Testing – Decibels (OHSU)	Listing 42
	Listing 16.2.6.1.3	Full-field Stimulus Testing – Log Units (UPenn)	Listing 43

	Listing 16.2.6.1.4	Full-field Stimulus Testing – Log Units (OHSU)	Listing 44
	Listing 16.2.6.2.1	Best-corrected Visual Acuity – logMAR	Listing 45
	Listing 16.2.6.2.2	Best-corrected Visual Acuity – ETDRS letters	Listing 46
	Listing 16.2.6.3.1	TPLR Amplitude (UPenn)	Listing 48
	Listing 16.2.6.3.2	TPLR Response Threshold (UPenn)	Listing 49
	Listing 16.2.6.3.3	Pupillometry – EDC	Listing 47
	Listing 16.2.6.3.4	Pupillometry – MERIT (OHSU)	Listing 50
	Listing 16.2.6.4.1	Oculomotor Instability	Listing 51
	Listing 16.2.6.5.1	Photoaversion	Listing 52
	Listing 16.2.6.6.1	Low-luminance Visual Acuity	Listing 53
	Listing 16.2.6.7.1	Optical Coherence Tomography – EDC	Listing 54
	Listing 16.2.6.7.2	Optical Coherence Topography – MERIT	Listing 55
	Listing 16.2.6.7.3	Bleb Optical Coherence Tomography – MERIT	Listing 56
	Listing 16.2.6.8.1	NEI Visual Function Questionnaire-25 Results	Listing 57
	Listing 16.2.6.8.2	Cardiff Visual Ability Questionnaire for Children Results	Listing 58
	Listing 16.2.6.9.1	Patient’s Experience Due to Changes in Vision (PECV) Questionnaire	Listing 59
	Listing 16.2.6.10.1	Mobility Testing Results (UPenn)	Listing 60
16.2.7 - Adverse Event Listings	Listing 16.2.7.1	Treatment-emergent Adverse Events	Listing 10
	Listing 16.2.7.2	TEAEs Leading to Death	Listing 11
	Listing 16.2.7.3	Serious TEAEs	Listing 12
	Listing 16.2.7.4	TEAEs Leading to Treatment Discontinuation	Listing 13
	Listing 16.2.7.5	Adverse Events of Special Interest (AESIs)	Listing 14
	Listing 16.2.7.6.1	AESIs and SAEs for Subjects with Positive ADA to AAV5 Result at Baseline	Listing 30
	Listing 16.2.7.6.2	AESIs and SAEs for Subjects with Positive ADA to RetGC1 Result at Baseline	Listing 31
	Listing 16.2.7.6.3	AESIs and SAEs for Subjects with Detected ELISpot to AAV5 Result at Baseline	Listing 32
	Listing 16.2.7.6.4	AESIs and SAEs for Subjects with Detected ELISpot to RetGC1 Result at Baseline	Listing 33

	Listing 16.2.7.6.5	AESIs and SAEs for Subjects with Treatment-Emergent Positive ADA to AAV5 Result	Listing 34
	Listing 16.2.7.6.6	AESIs and SAEs for Subjects with Treatment-Emergent Positive ADA to RetGC1 Result	Listing 35
	Listing 16.2.7.6.7	AESIs and SAEs for Subjects with Treatment-Emergent Positive ELISpot to AAV5 Result	Listing 36
	Listing 16.2.7.6.8	AESIs and SAEs for Subjects with Treatment-Emergent Positive ELISpot to RetGC1 Result	Listing 37
16.2.8 - Listing of Individual Laboratory Measurements by Subject	Listing 16.2.8.1.1	Vital Signs	Listing 38
	Listing 16.2.8.1.2	Subjects with Vital Signs Outside of Normal Range	Listing 40
	Listing 16.2.8.1.3	Subjects Having Vital Signs PCSA	Listing 39
	Listing 16.2.8.2.1	Hematology Values	Listing 20
	Listing 16.2.8.2.2	Chemistry Values	Listing 21
	Listing 16.2.8.2.3	Urinalysis Values	Listing 22
	Listing 16.2.8.2.4	Subjects with Laboratory Parameters Outside of Normal Range	Listing 19
	Listing 16.2.8.2.5	Subjects Having Laboratory PCSA	Listing 18
	Listing 16.2.8.3.1	ADA AAV5 and RetGC1 Results	Listing 23
	Listing 16.2.8.3.2	ELISpot to AAV5 Results	Listing 24
	Listing 16.2.8.3.3	ELISpot to RetGC1 Results	Listing 25
	Listing 16.2.8.3.4	Subjects with Treatment-Emergent Positive ADA to AAV5	Listing 26
	Listing 16.2.8.3.5	Subjects with Treatment-Emergent Positive ADA to RetGC1	Listing 27
	Listing 16.2.8.3.6	Subjects with Treatment-Emergent Positive ELISpot to AAV5	Listing 28
	Listing 16.2.8.3.7	Subjects with Treatment-Emergent Positive ELISpot to RetGC1	Listing 29
	Listing 16.2.8.4	Results of Ocular Examinations (Slit Lamp Examination and Ophthalmoscopy)	Listing 15
	Listing 16.2.8.5	Fundus Photography	Listing 17
	Listing 16.2.8.6	Intraocular Pressure	Listing 16