Statistical Analysis Plan for Interventional Studies

Sponsor Name: Vyluma, Inc.

Protocol Number: CP-NVK002-0001
Protocol Title: CHILDHOOD ATROPINE FOR MYOPIA PROGRESSION (CHAMP): A 3-ARM RANDOMIZED, DOUBLE-MASKED, PLACEBO-CONTROLLED, PHASE 3 STUDY OF ATROPINE SULFATE OPHTHALMIC SOLUTION 0.01% AND 0.02%

Protocol Version and Date: (DD-Mmm-YYYY): Amendment 5 14-Jun-2021

Syneos Health Project Code: 1010025

Authors: Wayne Schuck, Principal Biostatistician

Revision History

Version #	Date (DD-Mmm-YYYY)	Document Owner	Revision Summary
0.1	17-Jan-2020	W. Schuck	Initial Release Version
0.2	17-Jul-2020	W. Schuck	Complete update of efficacy analysis due to pending. protocol amendment. Specifically, designation of secondary and exploratory analyses and order of analysis. Clarification on how to treat missing data due to COVID-19.
0.3	21-Aug-2020	W. Schuck	Updated based on Nevakar comments
0.4	15-Sep-2020	W. Schuck	Updated based on Nevakar comments Update of visit windows Clarification of multiple imputation for tipping point analysis
0.5	25-Sep-2020	W. Schuck	Updated based on Nevakar comments Additional clarification of multiple imputation for tipping point analysis
1.0	28-Sep-2021	W. Schuck	Updated Per Vyluma comments and Amendment 5. Added sensitivity analysis for proportion of subjects with less than 0.50D myopia progression (SER) at Month 36 Update Treatment compliance for use with added treatment diary Added summary of switching dosing from parent to subject Added section for modified Amblyopia Treatment Index Added section for Rebound Assessment Based on the Change from Stage 2 Baseline
1.1	08-Apr-2022	W. Schuck	Apply normalization or SER for analysis, summary, and listings Updated estimate statements to include all scheduled visit measurements Changed “Adverse Events of Special Interest” to “Adverse Events Associated with Antimuscarinic Function” Updated list of ophthalmological Adverse Events Associated with Antimuscarinic Function

Version #	**Date** (DD-Mmm-YYYY)	**Document Owner**	**Revision Summary**
1.2	18-May-2022	W. Schuck	Updated Per Vyluma comments. Added Supportive Analysis using subject composite endpoint Update TEAE definitions to clarify Stage 1 and Stage 2 definitions Revised the description of the primary and secondary responder analysis outputs as "between-treatment group difference in the proportion of subjects' eyes who show less than 0.5D myopia progression (SER) from baseline"
1.3	19-Jun-2022	W. Schuck	Updated Subgroup analyses Updated Treatment-Emergent Adverse Event Definition Clarification of multiple imputation for tipping point analysis Misc. updates per Vyluma
1.4	28-Jun-2022	W. Schuck	Misc. updates per Vyluma
2.0	29-Jun-2022	W. Schuck	Signed as Stable
2.1	17-Aug-2022	W. Schuck	Addition of subgroup analyses of primary endpoint Addition of Adverse Event tables by sex, age, and race Update of table numbering
3.0	24-Aug-2022	W. Schuck	Finalized

I confirm that I have reviewed this document and agree with the content.

Approvals

Syneos Health Approval

Wayne Schuck, Principal Biostatistician	Wayne Schuck *Electronically signed by: Wayne Schuck Reason: I am the author Date: Aug 30, 2022 13:40 EDT*	Aug 30, 2022
Name, Title Lead Biostatistician	Signature	Date (DD-Mmm-YYYY)
David Dai, Principal Biostatistician	*Electronically signed by: David Dai Reason: I am the reviewer Date: Aug 30, 2022 13:49 EDT*	Aug 30, 2022
Name, Title Senior Statistical Reviewer	Signature	Date (DD-Mmm-YYYY)
Myra Yao, Associate Director, Biostatistics	*Electronically signed by: Myra Yao Reason: I am the reviewer Date: Aug 30, 2022 13:02 CDT*	Aug 30, 2022
Name, Title Senior Statistical Reviewer	Signature	Date (DD-Mmm-YYYY)

Vyluma, Inc. Approval

Simon Chandler, Vice President, Ophthalmology	Simon Chandler *Electronically signed by: Simon Chandler Reason: I am the approver Date: Aug 30, 2022 15:52 EDT*	Aug 30, 2022
Name, Title Sponsor Contact	Signature	Date (DD-Mmm-YYYY)

Table of Contents

1. Glossary of Abbreviations

Abbreviation	Description
AE	Adverse Event
ATC	Anatomical Therapeutic Chemical
ATI	Amblyopia Treatment Index
BCVA	Monocular Best-Corrected Visual Acuity
BMI	Body Mass index
BDRM	Blinded Data Review Meeting
CI	Confidence Interval
CRA	Clinical Research Associate
D	Diopter
eCRF	Electronic Case Report Form
EC	Ethics Committee
EOS	End Of Study
GPP	Good Pharmacoepidemiology Practice
ICH	International Conference on Harmonization
ICF	Informed Consent Form
IRB	Institutional Review Board
mATI	Modified Amblyopia Treatment Index
IRT	Interactive Response Technology
IQR	Inter Quartile Range
ITT	Intent-to-Treat
Max	Maximum
MCMC	e
MedDRA	Medical Dictionary for Regulatory Activities
Min	Minimum
mITT	Modified Intent-to-Treat
mPPS	Modified Per Protocol Set
N/A	Not Applicable
PT	Preferred Term

Abbreviation	Description
PPS	Per Protocol Set
QC	Quality Control
OTC	Over-The-Counter
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SER	Spherical Equivalent Refraction
SOC	System Organ Class
SOP	Standard Operating Procedure
SLE	Slit-Lamp Examination
SS	Safety Set
TEAE	Treatment-emergent Adverse Event
TFL	Table, Figure, and Listing
VD	Vertex Distance

2. Purpose

The purpose of this statistical analysis plan (SAP) is to ensure that the data listings, summary tables and figures which will be produced, and the statistical methodologies that will be used, are complete and appropriate to allow valid conclusions regarding the study objectives.

2.1. Responsibilities

Syneos Health will perform the statistical analyses and are responsible for the production and quality control (QC) of all tables, figures, and listings.

2.2. Timings of Analyses

The primary analysis of Stage 1 safety and efficacy is planned after all subjects complete the final study visit of Stage 1 or terminate early from the study (see Sec 3.3 and 3.6 for definition of Stages 1 and 2).

Additional analyses of Stage 2 safety and efficacy is planned after all subjects complete the final study visit of Stage 2 or terminate early from the study.

3. Study Objectives

3.1. Primary Objective

The primary objective of the study is to evaluate the safety and efficacy of 2 concentrations of Atropine Sulfate Ophthalmic Solution (0.01% and 0.02%) compared to Vehicle (placebo) for slowing the progression of myopia in children over a 3-year treatment period.

3.2. Exploratory Objective

The exploratory objective of the study is to observe the safety and efficacy in subjects re-randomized to 1 year of treatment with Atropine Sulfate Ophthalmic Solution, 0.01% or 0.02%, or Vehicle following 3 years of treatment in children with progressive myopia.

3.3. Brief Description

This will be a 3-arm randomized, multicenter, double-masked, placebo-controlled, Phase 3 study conducted in 2 stages. Stage 1 is a safety and efficacy phase of 3 years (36 months) in duration, during which subjects will be allocated one of three study medications. Stage 2 is a randomized cross-over phase of 1 year (12 months) in duration, for the purpose of observing the effects of changing or stopping treatment. During Stage 2, subjects will be re-randomized to receive 1 of the 3 study medications with subjects initially randomized to Vehicle only eligible for randomization to 0.01% or 0.02% Atropine Sulfate Ophthalmic Solution. Subjects (aged 3 to ≤ 17.0 years) will enter the study with myopia spherical equivalent refraction (SER) of at least -0.50 D and no greater than -6.00 D myopia in each eye as measured by cycloplegic autorefraction and following successful eligibility screening at the Screening/Baseline visit will be randomized to one of the 3 treatment groups in a 2:2:3 ratio. The randomization will be stratified twice: (1) by age at randomization (subjects < 9 years; subjects ≥ 9 years) and by (2) refractive error (less myopic: SER -0.50 to -3.00 D; more myopic: one or more eyes with SER -3.01 to -6.00 D). The stratification is used to balance these characteristics across the 3 treatment groups.

The target number of subjects to be randomized into the 6-year to 10-year age group (436), the primary efficacy population. Approximately 483 subjects over all eligible ages will be enrolled. Enrollment will proceed until 436 subjects aged 6 to 10 years have been randomized and at least 483 subjects overall have been randomized. Enrollment may be closed to subjects age ≥ 11 years following enrollment of 50 subjects in this age group to avoid over-enrollment into the study.

3.4. Subject Selection

Study subjects will be children, male or female, aged 3 to ≤ 17.0 years at the time of enrollment, with myopia spherical equivalent refraction (SER) of at least -0.50 D and no greater than -6.00 D in each eye, astigmatism of no more than -1.50 D in each eye, and anisometropia (SER) of < 1.50 D as measured by cycloplegic autorefraction.

3.4.1. Inclusion Criteria

1. Children (female and male) aged 3 to ≤ 17.0 years.

2. Myopia SER of at least -0.50 D and no greater than -6.00 D myopia in each eye as measured by cycloplegic autorefraction.

3. If present, astigmatism of no more than -1.50 D in each eye as measured by cycloplegic autorefraction.

4. Anisometropia SER of < 1.50 D as measured by cycloplegic autorefraction.

5. Normal intraocular pressure of < 21 mm Hg in each eye.

6. Distance vision correctable to at least 0.1 logMAR or 20/25 Snellen equivalent in each eye.

7. Female subjects of childbearing potential (post menarche) must have a negative urine pregnancy test at screening.

8. Subject's parent or legal guardian must provide informed consent on behalf of the subject, and the subject should provide assent when applicable, per Institutional Review Board (IRB)/Ethics Committee (EC) guidelines. If a subject becomes an adult (depending on country regulations) during the study, they will need to sign an informed consent form (ICF) to continue in the study.

3.4.2. Exclusion Criteria

1. Allergy to atropine or any of the excipients of the eye drops.

2. Current or history of amblyopia or manifest strabismus including intermittent tropia.

3. Heart rate is persistently (for more than 10 minutes) > 120 beats per minute at screening/baseline.

4. History of any disease or syndrome that predisposes the subject to severe myopia (e.g., Marfan syndrome, Stickler syndrome, retinopathy of prematurity).

5. History in either eye of abnormal ocular refractive anatomy (e.g., keratoconus, lenticonus, spherophakia).

6. History in either eye of previous intraocular or ocular laser/non-laser surgery.

7. Current or history of glaucoma; anatomic narrow anterior chamber angles.

8. Serious systemic illness that, in the Investigator's opinion, would render the subject ineligible.

9. Chronic use of any topical or systemic antimuscarinic/anticholinergic medications (e.g., atropine, scopolamine, tropicamide) within 21 days prior to screening and/or anticipated need for chronic use during the study period (i.e., more than 7 consecutive days in 1 month or more than 30 total days in 1 year). Use of cycloplegic drops for dilated ocular exam are allowable.

10. Chronic use (more than 3 days per week) of any topical ophthalmic medications (prescribed or over-the-counter [OTC]) other than the assigned study medication. Use of artificial tears is allowed but may not be used within 2 hours of administration of study medication.

11. The anticipated need to use chronic ophthalmic or systemic oral corticosteroids during the study. Intranasal, inhaled, topical dermatologic, intra-articular, perianal steroids, and short-term oral steroids (i.e., < 2 weeks) are permitted.

12. Prior myopia control treatment including orthokeratology, bifocal contact lenses, or progressive addition spectacle lenses. The only allowable prior treatments are myopic correction in the form of single-vision eyeglasses and/or single-vision or toric soft contact lenses.

13. Preplanned hospitalization during the study period. (Note: The study period begins at the time of randomization.)

14. Unwilling or unable to complete study procedures or to be followed up for the 48-month duration

of the study.

15. Participation in any other study of investigational therapy during the study period or within the last 30 days.

16. History of any substance abuse (excessive or habitual use of alcohol and/or drug including nicotine) and not willing to abstain from these substance(s) during the 4-year study period.

17. Female subjects who are pregnant, nursing, or plan to become pregnant at any time during the study.

18. Employees of the study site and their family members are not permitted to participate as subjects in the study. Immediate family is defined as a spouse, parent, child, or sibling, whether biological or legally adopted.

19. Current or history of significant or severe damage to the cornea.

3.5. Determination of Sample Size

For the purposes of the study and identifying sample size, a responder is defined as a subject with a > -0.50 D myopia progression (SER) from baseline at a given time point.

3.5.1. Atropine Sulfate Ophthalmic Solution, 0.02%

A Fisher's exact test with a 0.05 two-sided significance level will have 95% power to detect the difference between an Atropine Sulfate Ophthalmic Solution, 0.02% responder proportion of 0.25, and a Vehicle responder proportion of 0.07 when the sample sizes are 136 and 91, respectively.

3.5.2. Atropine Sulfate Ophthalmic Solution, 0.01%

A Fisher's exact test with a 0.05 two-sided significance level will have 90% power to detect the difference between an Atropine Sulfate Ophthalmic Solution, 0.01% responder proportion of 0.25, and a Vehicle responder proportion of 0.07 when the sample size in each group is 91.

3.6. Treatment Assignment & Blinding

3.6.1. Stage 1

In Stage 1, subjects will be randomized in a 2:2:3 ratio of vehicle: Atropine Sulfate Ophthalmic Solution, 0.01%: Atropine Sulfate Ophthalmic Solution, 0.02%. The target number of subjects to be randomized into the 6- to 10-year age group (436), the primary efficacy population, will be:

- Vehicle (placebo): 125
- Atropine Sulfate Ophthalmic Solution, 0.01%: 125
- Atropine Sulfate Ophthalmic Solution, 0.02%: 186

Approximately 483 subjects over all eligible ages will be enrolled, resulting in the following numbers of subjects in each arm:

- Vehicle (placebo): 138
- Atropine Sulfate Ophthalmic Solution, 0.01%: 138
- Atropine Sulfate Ophthalmic Solution, 0.02%: 207

The randomization will be stratified twice: (1) by age at randomization (subjects < 9 years; subjects ≥ 9 years) and by (2) refractive error (less myopic: SER -0.50 to -3.00 D; more myopic: one or more eyes with SER -3.01 to -6.00 D). The stratification is used to balance these characteristics across the 3 treatment groups. Enrollment will proceed until 436 subjects aged 6 to 10 years have been randomized and at least 483 subjects overall have been randomized. Enrollment may be closed to subjects ≥ 11 years following enrollment of 50 subjects in this age group to avoid over-enrollment into the study.

If subjects meet eligibility criteria at the Screening/Baseline visit (Day 0), subjects will be randomly assigned to masked study medication. Study sites will utilize the IRT to assign kits to subjects. The treatment kit number will be recorded in the subject's eCRF. Study medication from the Interactive Response Technology (IRT)-assigned kit will be dispensed to the subject/subject's parent or guardian for dosing that evening. Subjects will return to the study site at 3-month intervals to return their study medication and their next assigned study medication kit will be dispensed. It is preferred that the subject attend every visit, but the parent/guardian may attend a 3-month visit without the subject if necessary. Both the subject and parent/guardian must be present at all 6-month safety and efficacy visits.

The study will be double masked. The study medication will be provided in identical-appearing laminated pouches with no labeling indicating the identity of the study group or the contents of the unit dose ampules. The laminated pouches will contain identical-appearing unit dose ampules. Study subjects, Investigators and staff, and study management personnel will be masked to the identity of treatment until after the final database lock of Stage 1. Subjects, investigators, and study site personnel will remain blinded to Stage 1 treatment until Stage 2 is completed and database is locked.

3.6.2. Stage 2

At initiation of Stage 2 of the study, all subjects will be re-randomized to receive 1 of 3 study medications. Subjects who were randomized to 0.01% or 0.02% Atropine Sulfate Ophthalmic Solution during Stage 1 will be re-randomized a in a 1:1:1 ratio to one of the 3 treatment arms (Vehicle: Atropine Sulfate Ophthalmic Solution, 0.01%: Atropine Sulfate Ophthalmic Solution, 0.02%), and subjects who were randomized to Vehicle during Stage 1 will be re-randomized in a 1:1 ratio to active treatment (Atropine Sulfate Ophthalmic Solution, 0.01%: Atropine Sulfate Ophthalmic Solution, 0.02%). The randomization list will be created by an independent biostatistician and sites will utilize the IRT to assign subject kits as per the procedures delineated for Stage 1. Study medication during Stage 2 will continue to be double masked.

3.7. Administration of Study Medication

First Dose of Study Medication: The subject (or caregiver if the subject is not able to self-administer the medication) will administer 1 full drop of the study medication into each eye from a single unit dose ampule at bedtime the evening of the randomization visit.

Each subsequent evening of dosing, the subject or caregiver will administer one full drop into each eye from a single new ampule and close the eyes gently for 30 seconds. The used ampule will be placed in the provided receptacle for return to the study site.

Subjects and/or their parent/guardian should make every effort not to miss administering doses during the study. Should a subject miss a dose, then the subject should wait until the following evening and then continue with his/her regular dosing schedule. Subject should not administer more than 1 dose to each eye per day.

Subjects or their parent/guardian will return all unopened study medication materials at the next office

visit. Site personnel will conduct treatment adherence assessment procedures for the last study period and dispense study medication for the next 3-month study period. At the Month 48 visit, final study drug accountability will be conducted. The Month 48 visit will mark the end of study treatment; no further study medication will be dispensed at this visit.

3.8. Study Procedures and Flowchart

During Stage 1, office visits will occur at Screening/Baseline, Months 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, and 36.

During the Three-Month Visits (Months 3, 9, 15, 21, 27, 33), subjects and their parent/guardian will return to the study site with their randomized study medication for an evaluation of treatment adherence. While it is preferred that the subject attend every visit, the parent/guardian may attend a 3-month visit without the subject if necessary. Sites will update concomitant medications, conduct AE assessment, dispense study medication, and perform treatment adherence assessment (i.e., study medication accountability).

During the Stage 1 Six-Month Visits (Months 6, 12, 18, 24, and 30), subjects and their parent/guardian will return to the study site with their randomized study medication for an evaluation of treatment adherence. Subjects will undergo a measurement of height (yearly), weight (yearly), HR, BCVA measurement (distance and near), photopic pupil size measurement, slit-lamp examination (SLE), tonometry, dilated fundus examination (yearly), cycloplegic autorefraction, axial length and, if possible, crystalline lens thickness. Sites will update concomitant medications, conduct AE assessment, dispense study medication, and perform treatment adherence assessment.

During the Month 36 visit, subjects and their parent/guardian will return to the study site with their randomized study medication for an evaluation of treatment adherence. Subjects will undergo a measurement of height, weight, HR, BCVA measurement (distance and near), photopic pupil size measurement, SLE, tonometry, dilated fundus examination, cycloplegic autorefraction, axial length and, if possible, crystalline lens thickness. Subjects will then be re-randomized. Sites will update concomitant medications, conduct AE assessment, dispense randomized study medication for the randomized crossover stage (Stage 2), and perform treatment adherence assessment.

For the Stage 1 Telephone Checks - (Months 1, 2, 4.5, 7.5, 10.5) sites will contact subjects or their parent/guardian by telephone at the end of Month 1 and Month 2 and then midway between office visits during the initial year of the study to collect information regarding AEs and treatment adherence. Telephone checks can be continued or reinstated at any time during the study to assist with maintaining protocol and treatment adherence.

Stage 2 begins during the Stage 1 Month 36 visit. During Stage 2, office visits will occur at Months 36, 39, 42, 45, and 48.

During Stage 2 Three-Month Visits (Months 39 and 45), subjects and their parent/guardian will return to the study site with their randomized study medication for an evaluation of treatment adherence (as in Stage 1, it is preferred that the subject attend every visit, but the parent/guardian may attend a 3-month visit without the subject if necessary). Sites will update concomitant medications, conduct AE assessment, dispense study medication, and perform treatment adherence assessment.

During Stage 2 Six-Month Visit (Month 42), subjects and their parent/guardian will return to the study site with their randomized study medication for an evaluation of treatment adherence. Subjects will undergo a measurement of HR, BCVA measurement (distance and near), photopic pupil size measurement, SLE, tonometry, cycloplegic autorefraction, axial length, and, if possible, crystalline lens thickness. Sites will update concomitant medications, conduct AE assessment, dispense study medication, and perform treatment adherence assessment.

At the Month 48 end of study (EOS) visit, subjects and their parent/guardian will return to the study site

with their randomized study medication for an evaluation of treatment adherence. Subjects will undergo a measurement of height, weight, HR, BCVA measurement (distance and near), photopic pupil size measurement, SLE, tonometry, dilated fundus examination, cycloplegic autorefraction, axial length, and, if possible, crystalline lens thickness. Sites will update concomitant medications, conduct AE assessment, and perform treatment adherence assessment.

Every effort should be made to keep subjects in the study and conduct all study visits as scheduled. If a subject is discontinued from study medication before the Month 48 visit, then all Month 48 (EOS) procedures should be performed at the visit the subject is discontinued.

Full details of each visit can be found in Table 2: Schedule of Procedures in the protocol.

4. Endpoints

4.1. Primary Efficacy Endpoint

The primary efficacy endpoint is the overall between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) difference in the proportion of subjects' eyes who show less than 0.5 D myopia progression (SER) from baseline at the Month 36 visit.

4.2. Secondary Efficacy Endpoints

The secondary efficacy endpoints will consist of:

1. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) difference in the mean change from baseline in SER at the Month 36 visit.

2. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) difference in the proportion of subjects' eyes who show less than 0.5 D myopia progression (SER) from baseline at the Month 36 visit.

3. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) difference in the mean change from baseline in SER at the Month 36 visit.

4. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) difference in the mean change from baseline in axial length at the Month 36 visit.

5. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) difference in the mean change from baseline in axial length at the Month 36 visit.

4.3. Tertiary Endpoints

Tertiary endpoints will consist of:

1. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) difference in the proportion of subjects' eyes who show less than 0.5 D myopia progression (SER) from baseline at the Month 24 and Month 12 visits.

2. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) difference in the mean change from baseline in SER at the Month 24 and Month 12 visits.

3. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) difference in the proportion of subjects' eyes who show less than 0.5 D myopia progression (SER) from baseline at the Month 24 and Month 12 visits.

4. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) difference in the mean change from baseline in SER at the Month 24 and Month 12 visits.

5. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) difference in the proportion of subjects' eyes who show less than 0.75 D myopia progression (SER) from baseline at the Month 36 visit.

6. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) difference in the proportion of subjects' eyes who show less than 0.75 D myopia progression (SER) from baseline at the Month 36 visit.

7. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) difference in the time to change from baseline in myopia of -0.75 D SER.

8. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) difference in the time to change from baseline in myopia of -0.75 D SER

9. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) difference in the mean number of new prescriptions given after the start of treatment due to progression through the Month 36 visit.

10. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) difference in the mean number of new prescriptions given after the start of treatment due to progression through the Month 36 visit.

11. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) difference in the proportion of subjects who progressed from baseline to high myopia (SER -6.00 D or more myopic) at the Month 36 visit.

12. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) difference in the proportion of subjects who progressed from baseline to high myopia (SER -6.00 D or more myopic) at the Month 36 visit.

13. Interaction between demographic variables (age 6 – 8 years versus 9 – 10 years; baseline SER -0.50 to -3.00 D versus more myopic than -3.00 D SER; Asian versus non-Asian; dark irides versus light irides, region (U.S. versus E.U.); female versus male and SER at randomization.

14. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) difference in the change from baseline in crystalline lens thickness at the Month 36 visit.

15. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) difference in the change from baseline in crystalline lens thickness at the Month 36 visit.

4.4. Exploratory Efficacy Endpoints

Exploratory endpoints will consist of:

1. Between-treatment group difference in the mean change from study baseline in SER at the Month 48 visit for all subjects who respond in the Atropine Sulfate Ophthalmic Solution treatment groups at the Month 36 visit.

2. Between-treatment group difference in the mean change from Stage 2 baseline (Month 36) in SER at the Month 48 visit for all subjects who respond in the Atropine Sulfate Ophthalmic Solution treatment groups at the Month 36 visit.

3. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle and Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) Difference in the Proportion of Subjects' Eyes with Higher Myopia (SER <= -3.00) who Show less than 0.75 D Myopia Progression (SER) From Baseline at the Month 36 Visit

5. Analysis Sets

5.1. Enrolled Set

The Enrolled Set will include all subjects enrolled. Unless specified otherwise, this set will be used for subject listings and summaries of subject disposition.

5.2. Safety Set

The Safety Set (SS) will include all subjects who were administered at least one dose of study medication for a given stage. Stage 1 Safety Set is defined by administration of at least one dose of study medication in Stage 1. Stage 2 Safety Set is defined by administration of at least one dose of study medication in Stage 2. Subjects will be analyzed according to first treatment received for each stage. In the case of listings or tables that present data from both stages, then treatment sequence will be used. The SS will be used for all analyses of safety endpoints and for the presentation of subjects in all subject listings.

5.3. Intent-to-Treat Set

The Intent-to-Treat (ITT) Set will include all randomized subjects for a given stage. Stage 1 ITT Set is defined by randomization of a subject into a Stage 1 treatment. Stage 2 ITT Set is defined by randomization of a subject into a Stage 2 treatment. Subjects will be analyzed according to randomized treatment. The ITT Set will be used for all analyses of efficacy endpoints, unless otherwise specified, and for the presentation of subjects in all subject listings.

5.4. Modified Intent-to-Treat

The Modified Intent-to-Treat (mITT) Set will include all randomized subjects, for a given stage, aged 6 to 10 years at the time of randomization in Stage 1. Stage 1 mITT Set is defined by randomization of a subject, aged 6 to 10 years at the time of randomization in Stage 1, into a Stage 1 treatment. Stage 2 mITT Set is defined by randomization of a subject, aged 6 to 10 years at the time of randomization in Stage 1, into a Stage 2 treatment. This will be the population for the primary efficacy analyses. Subjects will be analyzed according to randomized treatment.

5.5. Per Protocol Set

The Per Protocol Set (PPS) will include all subjects who remain in the study through end of stage and have no major or critical protocol violations. Stage 1 PPS requires subjects to remain in the study through Month 36. Stage 2 PPS requires subjects to remain in the study through Month 48. This will be the population for selected efficacy analyses. Subjects will be analyzed according to randomized treatment. Criteria for inclusion in the PPS includes the following important Protocol deviations for which subjects are to be included within each analysis set are determined at a BDRM (see 5.7) before unblinding.

5.6. Modified Per Protocol Set

The Modified Per Protocol Set (mPPS) will include all subjects in the PP analysis population in each stage who were aged 6 to 10 years at the time of randomization. This will be the population for selected efficacy analyses. Subjects will be analyzed according to randomized treatment.

5.7. Protocol Deviations

Protocol deviations will be collected throughout the study. All protocol deviations classified as Minor, Major, or Critical. Based on these classifications, subjects with Major or Critical deviations will be tentatively

identified as not in the PPS and Modified PPS. Listings of proposed analysis set designations and protocol deviations will be distributed to the sponsor for review.

Protocol deviations and analysis set assignments will be reviewed during a Masked Data Review Meeting (BDRM). Additional details of selection criteria, documentation, and scheduling of the BDRM to be provided for review will be described in the BDRM Preparation Plan.

6. General Aspects for Statistical Analysis

6.1. General Methods

- SAS® version 9.4 or newer is to be used for all analyses and outputs
- Unless otherwise specified, summaries will be presented for each treatment group by study stage
- Continuous variables will be summarized using the number of observations (n), mean, standard deviation (SD), median, minimum, and maximum. Due to the expected strong correlation between eyes within a subject, eye-related continuous variables, where the object of measure is subjects' eyes, will be summarized using the number of observations (n), mean, Inter Quartile Range (IQR), median, minimum, and maximum. Categorical variables will be summarized using number of observations (n), frequency, and percentages of subjects.
- All relevant subject data will be included in listings. All subjects entered into the database will be included in subject data listings.

6.2. Key Definitions

Treatment-emergent adverse events (TEAEs) of Stage 1 are defined as any new or worsening of existing adverse events that occur or worsen between the first dose date of Stage 1 and the last dose date of Stage 1.

TEAEs of Stage 2 are defined as any AE the occurs or worsens between the first dose date of Stage 2 and the last dose date of Stage 2.

First dose date for Stage 1 is defined as the first dose of study medication received after randomization in Stage 1.

First dose date for Stage 2 is defined as the first dose of study medication received after the Stage 1 last dose date and subject is re-randomized.

For subjects who did not receive study medication in a given stage, leave first dose date for that stage as missing. If the first dose date is missing and if the subject is randomized, impute the missing first dose date using the randomization date in the analysis of Time to Change from Baseline in Myopia Progression of -0.75D (see 8.3.7 and 8.3.8).

Baseline for Stage 1 is defined as the last measurement prior to first dose of study medication in Stage 1, If an adverse event starts or non-study medication taken on the day of first dose it will be treated as occurring after treatment started. All other planned measurements are presumed to occur prior to first dose of study medication.

Baseline for Stage 2 will be defined as latest results prior to start of study medication in Stage 2, which occurs the day after the Month 36 visit. The results of the Month 36 visit will act as the baseline for Stage 2.

6.3. Missing Data

Partial dates of medications will be imputed solely for the purpose of defining prior/concomitant status for medications and treatment emergence for adverse events. Dates will be defined using the hierarchy of derivations below.

- For missing start day where month and year are present, the start day will be set to the 1st of the month, unless the month and year are the same as the first dose month and year and the 1st of the month is before the first dose date, in which case, the start date will be set to the first dose date.

- For missing start day and month where year is present, the start day and month will be set to January 1st, unless the year is the same as the first dose year and January 1st is before the first dose date, in which case, the start date will be set to the first dose date.

- For missing end day where month and year are present, the end day will be set to the last day of the month, unless the month and year are the same as the subject study termination month and year, in which case, the end date will be set to the trial termination date.

- For missing end day and month, where year is present, the end date will be set to the trial termination date if the years are the same. If the trial termination year is greater than the end year, the end day and month will be set to December 31st.

Missing efficacy data will be addressed in the related subsection of 8 below.

6.4. Visit Windows

In order to adapt to changes in subjects going to the investigator's office due to COVID-19, visit windows will be applied to incorporate visits that are reported as unscheduled visits or are out of protocol specified visit window once subjects were able to return to the investigator's office. Visit windowing will be applied for all analyses results of eye examinations. Examples of applicable eye exams are cycloplegic autorefraction and, tonometry intraocular pressure.

There are two sets of visit windows that will be applied. A narrower set of visit windows to be used in any appropriate analyses of the PP Set and a broad set of visit windows for all other appropriate analyses.

The day included for a visit is provided in Table 1 and Table 2 below.

Table 1: Visit Window Schedule (except for analysis of PPS)

Visit	Scheduled Visit Day	Visit Window
Baseline	Day 1	≤ Day 1
Month 6	Day 182	Day 2- Day 273
Month 12	Day 365	Day 274 – Day 456
Month 18	Day 548	Day 457 – Day 639
Month 24	Day 731	Day 640 – Day 822
Month 30	Day 913	Day 823 – Day 1004
Month 36	Day 1096	Day 1005 – Day 1187
Month 42	Day 1278	Day 1188 – Day 1369
Month 48	Day 1461	≥ Day 1370

Table 2: Visit Window Schedule (for analysis of PPS)

Visit	Scheduled Visit Day	Visit Window (±28day except Month 36 visit, ±42 days for Month 36)
Baseline	Day 1	≤ Day 1
Month 6	Day 182	Day 154 - Day 210
Month 12	Day 365	Day 337 – Day 393
Month 18	Day 548	Day 520 – Day 576
Month 24	Day 731	Day 703 – Day 759
Month 30	Day 913	Day 885 – Day 941
Month 36	Day 1096	Day 1068 – Day 1124
Month 42	Day 1278	Day 1250 – Day 1306
Month 48	Day 1461	Day 1419 – Day 1503

In case 2 or more visits occur within a visit window, the closest visit to the scheduled visit will be used for summaries and analysis. If 2 visits are equidistant from the scheduled visit, then the later visit will be used.

Stage 1 is scheduled to run from Baseline until the Month 36 visit. Stage 1 will end when the subject leaves the study or completes their Month 36 visit, whichever is earlier. Stage 2 will begin on the day of first dose after re-randomization.

6.5. Pooling of Centres

This section is not applicable because centre/country is not included in the statistical model.

6.6. Subgroups

Subjects are randomized based on two stratifications. The first stratification is by age (subjects < 9 years; subjects ≥ 9 years); the second is by refractive error (less myopic: SER -0.50 to -3.00 D; more myopic: one or more eyes with SER-3.01 to -6.00 D). The primary and secondary analyses will be repeated for each stratification.

Additional subgroup exploratory analyses will be performed differences between select demographic variables (Asian versus non-Asian; dark irides versus light irides; female versus male) and change from baseline in SER at Month 12, Month 24, and Month 36.

7. Demographic, Other Baseline Characteristics and Medication

7.1. Subject Disposition and Withdrawals

Subject disposition will be presented for all subjects, which include the following:

- Number of subjects enrolled
- Number of screened and reason for screen failure
- Number (%) of subjects randomized for Stage 1
- Number (%) of subjects re-randomized for Stage 2

Among the randomized subjects, the following will be summarized

- Number (%) of subjects in the Stage 1 Safety Set
- Number (%) of subjects in the Stage 1 Intent-to-Treat Set
- Number (%) of subjects in the Stage 1 Modified Intent-to-Treat Set
- Number (%) of subjects in the Stage 1 Per-Protocol Set
- Number (%) of subjects in the Stage 1 Modified Per-Protocol Set
- Number (%) of subjects who completed the Stage 1
- Number (%) of subjects who discontinued treatment in Stage 1 and their reason
- Number (%) of subjects who discontinued study prematurely in Stage 1 and their reason
- Number (%) of subjects who continuing the study into Stage 2
- Number (%) of subjects in the Stage 2 Safety Set
- Number (%) of subjects in the Stage 2 Intent-to-Treat Set
- Number (%) of subjects in the Stage 2 Modified Intent-to-Treat Set
- Number (%) of subjects in the Stage 2 Per-Protocol Set
- Number (%) of subjects in the Stage 2 Modified Per-Protocol Set
- Number (%) of subjects who completed the study (Stage 2)
- Number (%) of subjects who discontinued treatment in Stage 2 and their reason
- Number (%) of subjects who discontinued study prematurely in Stage 2 and their reason

A separate by-subject listing of subject disposition and withdrawal will also be provided. Subjects who screen failed will be listed along with the date and reason for the screen failure.

Randomized subjects not included in an analysis set and their reason for exclusion will be summarized and listed.

7.2. Demographic and Other Baseline Characteristics

Demographics and other baseline characteristics will be summarized for the Safety Set by actual treatment and overall and for the ITT Set, the mITT Set, the PPS, and the mPPS by randomized treatment group and overall. Summary statistics and by-subject listings will be provided. The summary will be repeated for all subjects who enter Stage 2.

Demographics and baseline characteristics will include age, sex, ethnicity, race, weight, height, body mass index (BMI), age strata (< 9; >= 9 years), and refractive error (less myopic: SER -0.50 to -3.00 D; more myopic: one or more eyes with SER-3.01 to -6.00 D).
Age at Study day 1 = ((Study day 1) visit date - date of birth + 1) / 365.25 and truncated to complete years.

Height (in cm) = height (in inches) * 2.54

Weight (in kg) = weight (in lbs.) * 0.4536

BMI (kg/m^2) = Weight(kg)/[Height$(m)^2$]

7.3. Baseline Disease Characteristics

Baseline values for spherical equivalent refraction (SER), astigmatism, anisometropia, axial length, and crystalline lens thickness will be summarized using descriptive statistics for Safety Set by actual treatment, and for the ITT Set, the mITT Set, the PPS, and the mPPS by randomized treatment group and overall. Summary statistics and by-subject listings will be provided. The summary will be repeated for all subjects who enter Stage 2.

7.4. Medical History

A summary table of the number and percentage of subjects of ocular and other medical history by system organ class (SOC) and preferred term (PT) will be produced from the Safety Set. Medical history will be sorted alphabetically by SOC and in descending order of subjects per preferred term within each SOC.

All Medical history will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 20.1 or higher.

A separate by-subject listing of medical history will also be provided.

7.5. Medication

All prior and concomitant medications will be summarized based on classification using the Anatomical Therapeutic Chemical (ATC) classification and preferred drug name from the World Health Organization Drug Dictionary, version Sep2017, or later. Concomitant medications will be summarized for each stage separately.

A separate by-subject listing of medications will also be provided.

7.5.1. Prior Medication

Prior medications are defined as medications entered in the eCRF that either start, or end before the first dose of study medication. Prior medications will be summarized by ATC level 2 and preferred drug name for the Safety Population.

Prior medications which continue after first dose of study medication will also be classified as a concomitant medication

7.5.2. Concomitant Medication

Concomitant medications are defined as medication on the eCRF that are taken on or after or are ongoing at the start date of dosing for each stage. Concomitant medications will be summarized by ATC level 2 and preferred drug name for the Safety Set for each stage.

8. Efficacy

The primary and all secondary endpoints comprise a fixed sequence set of endpoints to be tested in the order given below. All statistical testing will be performed using a two-sided testing procedure with α=0.05. Summaries of change for Stage 2 will include change from baseline and change from Stage 2 baseline (Month 36).

The order for the fixed sequence of endpoints to be tested are:

1. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) difference in the proportion of subjects' eyes who show less than 0.5 D myopia progression (SER) from baseline at the Month 36 visit. (Primary Endpoint)

2. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) difference in the mean change from baseline in SER at the Month 36 visit.

3. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) difference in the proportion of subjects' eyes who show less than 0.5 D myopia progression (SER) from baseline at the Month 36 visits.

4. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) difference in the mean change from baseline in SER at the Month 36 visit.

5. Between-treatment group (Atropine Sulfate Ophthalmic Solution 0.02% versus Vehicle) difference in the mean change from baseline in axial length at the Month 36) visit,

6. Between-treatment group (Atropine Sulfate Ophthalmic Solution 0.01% versus Vehicle) difference in the mean change from baseline in axial length at the Month 36 visit.

Not all sites used the same Vertex distance (VD) in mm when measuring refraction with autorefractor. All averaged SER measurements for each participant used in tables and analyses will be normalized to a VD of 0 mm to the corneal plane. The normalization (Fannin 1987) will be applied using

$$SSSSSS_{nnnnnnnnnnnnnnnn} = \frac{100}{\left(\frac{100}{SSSSSS}\right) - \left(\frac{VVVV}{10}\right)}$$

where SER is the original SER from CRF.

The normalized SER will be used in all efficacy analyses for SER. SER values for randomization and stratification will not be normalized. Baseline SER will be normalized for use in the statistical analyses of efficacy. Both the original SER (from CRF) and normalized SER will be presented in listings. The astigmatism value for eligibility purpose will not be normalized because normalization to the corneal plane from a spectacle plane will always lead to a less minus power and hence will not change astigmatism eligibility for enrolled participants

8.1. Primary Efficacy Endpoint and Analysis

8.1.1. Primary Efficacy Endpoint

The primary efficacy endpoint is the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) difference in the proportion of subjects' eyes who show less than 0.5 D myopia progression (SER) from baseline at the Month 36 visit.

Spherical equivalent refraction will be measured using cycloplegic autorefraction at Months 6, 12, 18, 24, 30, and 36. Subjects' eyes will be determined at each visit if they have a less than 0.5 D myopia progression (SER). All data collected through Month 36 will be used, regardless of when treatment is stopped. There will be no imputation for missing data; analysis will be conducted as observed.

The primary analysis will be performed using a Mixed Model based on the binomial distribution using a logit link function. Progression as the dependent variable, subject, treatment, visit, eye (left or right) and baseline age group (as randomized) and SER (as randomized) as independent variables and treatment by visit interaction term included. Random intercepts for subject and eye within subject will be included using variance components and compound symmetry covariance structures, respectively. The primary analysis will be performed using the mITT analysis set assuming data is missing at random.

```
proc glimmix data=master empirical method=quad;
  class subjid trtpn(ref='0') avisitn eye agegr1 sergr1;
  model eff(event='1') = trtpn avsitn eye agegrp1 sergrp1 trtpn*avisitn / dist=bin link=logit solution or;
  nloptions tech=nrridg maxiter=25;
  random intercept / subject=subjid type=vc;
  random intercept / subject=eye(subjid) type=cs;
  estimate '0.02% vs. Pbo Month 36' trtpn 0 1 -1 trtpn*avisitn 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0  0 0 -1;
```

The absolute risk difference and associated Wald 95% CI will also be presented at Month 36 using the following frequency procedure.

```
proc freq data=dat order=data;
  tables trtpn*eff / riskdiff(equal cl=wald);
```

Counts and percentage of subject' eyes progressing at each visit for each stage will be summarized. For the primary endpoint and associated secondary endpoints, Odds Ratios, 95% confidence interval (CI), and p-value will be provided along with an accompanying figure.

8.1.2. Supportive Analysis of Primary Endpoint

8.1.2.1. *Subject Composite Result*

The supportive efficacy endpoint is the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) difference in the proportion of subjects who show less than 0.5 D myopia progression (SER) from baseline at the Month 36 visit without factoring in both eyes within a subject. Subjects with at least one eye that shows less than 0.5 D myopia progression (SER) from baseline will be considered as responders. The supportive analysis will be performed using a Mixed Model based on the binomial distribution using a logit link function. Progression as the dependent variable, subject, treatment, visit, and baseline age group (as randomized) and SER (as randomized) as independent variables and treatment by visit interaction term included. Random intercept for subject will be included using variance components. The supportive analysis will be performed using the mITT analysis set assuming data is

missing at random. The supportive analysis is designed to reenforce the expectation of a strong correlation between eyes within a subject.

proc glimmix data=master empirical method=quad; for each visit
class subjid trtpn(ref='0') avisitn agegr1 sergr1;
*model eff(event='1') = trtpn avsitn agegrp1 sergrp1 trtpn*avisitn / dist=bin link=logit solution or;*
nloptions tech=nrridg maxiter=25;
random intercept / subject=subjid type=vc;
*estimate '0.02% vs. Pbo Month 36' trtpn 0 1 -1 trtpn*avisitn 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 -1;*

8.1.3. Sensitivity Analysis of the Primary Endpoint

Unless otherwise noted, all sensitivity analyses will be performed using the same method and model as the primary analysis.

8.1.3.1. *Subgroup Analyses*

For subgroup analyses, the analysis method will be the same as the primary efficacy analysis as described in 8.1.1 above, including sensitivity analyses using the statement:

estimate '0.02% vs. Pbo Month 12 Subgroup_Value1 trt01pn*avisitn1*Subgroup_Var
0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 -1 0 0 0 -1 0 0 0 0 0 0 0 0 0 0 0 / cl;

estimate '0.02% vs. Pbo Month 12 Subgroup Value2 trt01pn*avisitn1*Subgroup_Var
0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 -1 0 0/ cl

8.1.3.2. *On-Treatment Analysis*

The primary analysis uses all data from the study through Month 36. During that time if a subject stops treatment they are encouraged to remain in the study to the scheduled completion of the study at Month 48. The on-treatment analysis will exclude all data collected more than 4 weeks after last day of treatment.

The analysis method will be the same as the primary efficacy analysis as described in 8.1.1 above. There will be no imputation for missing data, analysis will be conducted as observed and data assumed to be missing at random.

8.1.3.3. *Modified Per Protocol Analysis*

A sensitivity analysis will be performed on the modified per protocol population (mPPS). There will be no imputation for missing data, analysis will be conducted as observed and data assumed to be missing at random. The analysis will be conducted using the same model as the primary efficacy analysis (as described in 8.1.1 above).

8.1.3.4. *Tipping Point Analysis*

A sensitivity analysis of the primary endpoint will be conducted by tipping point analysis: In the event, that statistical significance in favor of Atropine Sulfate Ophthalmic Solution, 0.02% is determined on the primary analysis. In this scenario, imputations will occur on the continuous value of spherical equivalent refraction (SER) which will then be used to determine treatment response. The imputation will be using Markov chain Monte Carlo (MCMC) methodology for non-monotone (intermittent) missing data (any missing data point with a non-missing data point following) followed by Monotone Regression

methodology for the remaining monotone missing data. The regression model for imputation will include, at a minimum, treatment, visit, eye (left or right) and baseline age group (as randomized) and SER (as randomized), race (Asian vs, non-Asian, see 8.3.13 below), eye color (dark irides versus light irides), and region (U.S. vs. E.U.). This set of imputations will be performed 10 times per evolution for a total of 100 imputations. Missing data from the placebo arm will be imputed according to the normalized placebo SER values, and treatment-related missing data on active arm imputation at each visit will adjusted from the normalized active SER values, up until the normalized placebo SER values at the respective visit in a minimum of 5 steps to assess if a tipping point exists between a statistically significant and a non-significant difference. The imputed datasets will be analyzed using the same model as the primary analysis. The results of these analyses will be combined into a single result using PROC MIANALYZE for each value of the shift. The objective is to determine whether a tipping point exists where the statistical significance between the Atropine Sulfate Ophthalmic Solution, 0.02% and placebo arm will no longer exist.

Treatment-related missing data are data missing because a subject terminates the study prior to the Month 36 visit for the following termination reasons:

- Subject withdrew consent
- Medical reason (AE)
- Physician decision to discontinue treatment
- Death
- Lack of efficacy

Non-treatment related missing data are data missing because a subject terminates the study prior to the Month 36 visit for the following termination reasons:

- Visit missed or telemedicine visit due to COVID-19
- Sponsor terminated study
- Lost to follow-up
- Pregnancy
- Other

8.1.4. COVID-19 Analyses

Data that is missing due to subject unable to go to the investigator's office due to COVID-19 are considered missing at random. The Mixed Model analysis being used in the primary analysis is known to be robust in dealing with data that is missing at random. Therefore, no additional sensitivity analyses will be performed involving data missing due to COVID-19.

8.1.5. Other Analysis of the Primary Endpoint

The primary analysis will be repeated for the ITT and PPS analysis sets and for each stratification level. Sensitivity analyses will be repeated for the ITT population only. There will be no imputation for missing data; analysis will be conducted as observed. The analysis will be conducted using the same model as the primary efficacy analysis (as described in 8.1.1 above).

As part of the sensitivity analyses for the primary efficacy analysis, the point estimate and 95% Wald confidence interval, for the absolute difference in the proportions of subjects with less than 0.50D myopia progression (SER) at Month 36 between the treatment groups without any models should be presented.

8.2. Secondary Efficacy Endpoint(s) and Analyses

Unless otherwise stated, all secondary analyses will use the mITT Set. The ITT Set will also be analyzed in the same manner as supportive analyses.

8.2.1. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) Difference in the Mean Change from Baseline in SER at the Month 36 Visit

A secondary analysis will be performed on the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) difference in the mean change from baseline in SER at the Month 36 visit.

The analysis will be performed using a mixed-effect model with a random intercept. Change from baseline as the dependent variable, treatment group, visit, eye (left or right) and baseline age group (as randomized) and baseline SER group (as randomized) as independent variables and treatment group by visit interaction term included. Degrees of freedom will be determined using the Kenward-Roger approximation. Random intercepts for subject and eye within subject will be included using unstructured covariance structures.

```
proc mixed data=xxxx noitprint method=REML order=internal;
  class subjid trtpn(ref='0') avisit eye agegr1 sergr1;
  model VA= trtpn avisit eye agegrp1 sergrp1 trtpn*avisit /solution DDFM=KR;
  random int/type=un sub=subjid;
  random int/type=un subject=subjid(eye);
  estimate '0.02% vs. Pbo Month 36' trtpn 0 1 -1 trtpn*avisitn 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0  0 0 -1/ cl;
```

Summary statistics and figure will be presented along with a full data listing by treatment group.

8.2.2. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) Difference in the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (SER) From Baseline at the Month 36 visit

A secondary analysis will be performed on the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) difference in the proportion of subjects' eyes who show less than 0.5 D myopia progression (SER) from baseline at the Month 36 visit. The analysis method will be the same as the primary efficacy analysis as described in 8.1.1 above, including sensitivity analyses using the updated statement:

```
estimate '0.01% vs. Pbo Month 36' trtpn 1 0 -1 trt01pn*avisitn 10 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 -1 0 / cl ;
```

8.2.3. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) Difference in the Mean Change from Baseline in SER at the Month 36 Visit

A secondary analysis will be performed on the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) difference in the mean change from baseline in SER at the Month 36 visits. The analysis method will be the same as the secondary efficacy analysis as described in 8.2.1 above using the updated statement:

```
estimate '0.01% vs. Pbo Month 36' trtpn 1 0 -1 trt01pn*avisitn 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 -1 0  0/ cl;
```

Summary statistics and figure will be presented along with a full data listing by treatment group.

8.2.4. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) Difference in the Mean Change from Baseline in Axial Length at Month 36

A secondary analysis will be performed on the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus vehicle) difference in the mean change from baseline in axial length at the Month 36 visit. The analysis method will be the same as the secondary efficacy analysis as described in 8.2.1 above.

Summary statistics will be presented along with a full data listing by treatment group.

8.2.5. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.01% Versus Vehicle) Difference in Mean Change from Baseline in Axial Length at the Month 36 Visit

A secondary analysis will be performed on the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.1% versus vehicle) change from baseline in axial length at the Month 36 visit. The analysis method will be the same as the secondary efficacy analysis as described in 8.2.1 above using the updated statement:

*estimate '0.01% vs. Pbo Month 36' trtpn 1 0 -1 trt01pn*avisitn 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 -1 0/ cl ;*

Summary statistics will be presented along with a full data listing by treatment group.

8.3. Tertiary Efficacy Endpoint(s) and Analyses

8.3.1. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.02% Versus Vehicle) Difference in the Proportion of Subjects' eyes who Show less than 0.5 D Myopia Progression (SER) From Baseline at the Month 24 and Month 12 visits

A tertiary analysis will be performed on between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% Versus Vehicle) difference in the proportion of subjects' eyes who show less than 0.5 D myopia progression (SER) from baseline at the Month 24 and Month 12 visits. The analysis method will be the same as the primary efficacy analysis as described in 8.1.1 above using the updated statements:

*estimate '0.02% vs. Pbo Month 12' trtpn 0 1 -1 trtpn*avisitn 0 0 0 0 0 0 1 0 0 0 0 0 -1 0 0 0 0 0*

*trt01pn*agegr1 0 0 0 1 0 -1;*
*estimate '0.02% vs. Pbo Month 24' trtpn 0 1 -1 trtpn*avisitn 0 0 0 0 0 0 0 0 1 0 0 0 0 0 -1 0 0 0;*

Summary statistics and figure will be presented along with a full data listing by treatment group.

8.3.2. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) Difference in the Mean Change from Baseline in SER at the Month 24 and Month 12 Visits

A tertiary analysis will be performed on the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus vehicle) difference in the mean change from baseline in SER at the Month 24 and Month 12 visits. The analysis method will be the same as the secondary efficacy analysis as described in 8.2.1 above using the updated statements:

*estimate '0.02% vs. Pbo Month 12' trtpn 0 1 -1 trtpn*avisitn 0 0 0 0 0 0 1 0 0 0 0 0 -1 0 0 0 0 0;*
*estimate '0.02% vs. Pbo Month 24' trtpn 0 1 -1 trtpn*avisitn 0 0 0 0 0 0 0 0 1 0 0 0 0 0 -1 0 0 0;*

Summary statistics and figure will be presented along with a full data listing by treatment group.

8.3.3. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) Difference in the Proportion of Subjects' Eyes Who Show less than 0.5 D Myopia Progression (SER) from Baseline at the Month 24 and Month 12 Visits

A tertiary analysis will be performed on the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus vehicle) difference in the proportion of subjects' eyes who show less than 0.5 D myopia progression (SER) from baseline at the 24 and Month 12 visits. The analysis method will be the same as the primary efficacy analysis as described in 8.1.1 above using the updated statements:

*estimate '0.01% vs. Pbo Month 12' trtpn 1 0 -1 trtpn*avisitn 1 0 0 0 0 0 0 0 0 0 0 -1 0 0 0 0 0 ;*
estimate '0.01% vs. Pbo Month 24' trtpn 1 0 -1 trtpn*avisitn 0 0 1 0 0 0 0 0 0 0 0 0 0 -1 0 0 0 ;

Summary statistics and figure will be presented along with a full data listing by treatment group.

8.3.4. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) Difference in the Mean Change from Baseline in SER at the Month 24 and Month 12 Visits

A tertiary analysis will be performed on the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01%) difference in the mean change from baseline in SER at the Month 24 and Month 12 visits. The analysis method will be the same as the secondary efficacy analysis as described in 8.2.1 above using the updated statements:

*estimate '0.01% vs. Pbo Month 12' trtpn 1 0 -1 trtpn*avisitn 1 0 0 0 0 0 0 0 0 0 0 -1 0 0 0 0 0;*
*estimate '0.01% vs. Pbo Month 24' trtpn 1 0 -1 trtpn*avisitn 0 0 1 0 0 0 0 0 0 0 0 0 0 -1 0 0 0;*

Summary statistics and figure will be presented along with a full data listing by treatment group.

8.3.5. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) Difference in the Proportion of Subjects' Eyes who Show less than 0.75 D Myopia Progression (SER) From Baseline at the Month 36 Visit

A tertiary analysis will be performed on difference in the proportion of subjects' eyes who show less than 0.75 D myopia progression (SER) from baseline at the Month 36 visit. The analysis method will be the same as the primary efficacy analysis as described in 8.1.1 above.

Summary statistics and figure will be presented along with a full data listing by treatment group.

8.3.6. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) Difference in the Proportion of Subjects' Eyes who Show less than0.75 D Myopia Progression (SER) From Baseline at the Month 36 Visit

A tertiary analysis will be performed on the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus vehicle) difference in the proportion of subjects' eyes who show less than 0.75 D myopia progression (SER) from baseline at the Month 36 visit. The analysis method will be the same as the primary efficacy analysis as described in 8.1.1 above using the updated statement:

*estimate '0.01% vs. Pbo Month 36' trtpn 1 0 -1 trtpn*avisitn 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 -1 0;*

Summary statistics will be presented along with a full data listing by treatment group.

8.3.7. Between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) Difference in the Time to Change from Baseline in Myopia Progression of -0.75 D SER

A tertiary analysis will be performed on the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus vehicle) difference in the time to change from baseline in myopia progression of -0.75 D SER.

The time to change in myopia progression of -0.75 D SER (days) = (first date with a change in myopia progression of -0.75 D or more – first date of treatment) +1. For subjects that were not observed to have a change in myopia progression of -0.75 D or more = Time to change in myopia progression of -0.75 D SER (days) [censored] = (Date of last known visit of Stage 1 – (first date of treatment) + 1.

The point estimate of the hazard ratios and the associated 95% confidence intervals will be obtained using the Cox proportional hazards regression model with fixed effects for treatment group, age at baseline, and baseline SER as covariates. An approximate Chi-square test based on Wald statistic will be used to compare treatment groups.

Summary statistics and associated survival curves (Kaplan-Meier estimates) will be presented along with a full data listing by treatment group.

Summary statistics will be presented along with a full data listing by treatment group.

8.3.8. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) Difference in Time to Change from Baseline in Myopia progression of -0.75 D SER

A tertiary analysis will be performed on the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus vehicle) difference in the time to change from baseline in myopia progression of -0.75 D SER. The analysis method will be the same as the tertiary efficacy analysis as described in 8.3.7 above.

Summary statistics will be presented along with a full data listing by treatment group.

8.3.9. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle) Difference in the Number of New Prescriptions Given After the Start of Treatment Due to Progression through the Month 36 visit

A tertiary analysis will be performed on the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus vehicle) difference in the number of new prescriptions given after the start of treatment due to progression through the Month 36 visit. The analysis method will be performed using the Cochran-Mantel-Haenszel row mean scores (ANOVA) statistic using the statement.

```
proc freq data=xxxx;
  tables Treatment*Prescriptions /cmh noprint;
run;
```

Summary statistics will be presented along with a full data listing by treatment group.

8.3.10. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) Difference in the Number of New Prescriptions Given After the Start of Treatment Due to Progression through the Month 36 visit

A tertiary analysis will be performed on the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus vehicle) difference in number of new prescriptions given after the start of treatment due to progression through the Month 36 visit. The analysis method will be performed using the Cochran-Mantel-Haenszel row mean scores (ANOVA) statistic using the statement.

```
proc freq data=xxxx;
  tables Treatment*Prescriptions /cmh noprint;
run;
```

Summary statistics will be presented along with a full data listing by treatment group.

8.3.11. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.02% Versus Vehicle) Difference in the Proportion of Subjects who Progressed to High Myopia (SER -6.00 D or more myopic) at the Month 36 Visit

A tertiary analysis will be performed on the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.2% versus vehicle) difference in the proportion of subjects who progressed to high myopia (SER -6.00 D or more myopic) at the Month 36 visit. Progression to high myopia is defined as either of a subject's eyes progressed to high myopia at any time during a visit window. The analysis method will be the same as the analysis as described in 8.3.12 below. Results will be presented as overall results and by baseline myopia stratification.

Summary statistics will be presented along with a full data listing by treatment group.

8.3.12. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) Difference in the Proportion of Subjects who Progressed to High Myopia (SER -6.00 D or more myopic) at the Month 36 Visit

A tertiary analysis will be performed on the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.1% versus vehicle) difference in the proportion of subjects who progressed to high myopia (SER -6.00 D or more myopic) at the Month 36 visit. Progression to high myopia is defined as either of a subject's eyes progressed to high myopia at any time during a visit window.

Results will be presented as results and by baseline myopia stratification. The overall analysis will be performed using a Mixed Model based on the binomial distribution using a logit link function. Progression as the dependent variable, subject, treatment, visit, and baseline age group (as randomized) and SER (as randomized) as independent variables, treatment by visit, treatment by SER (as randomized) and treatment by visit by SER (as randomized) interaction terms included. Random intercepts for subject will be included using variance components. The analysis will be performed using the mITT analysis set assuming data is missing at random.

```
proc glimmix data=master empirical method=quad;
   class subjid trtpn(ref='0') avisitn agegr1 sergr1;
   model eff(event='1') = trtpn avsitn agegrp1 sergrp1 trtpn*avisitn trtpn*sergr1 trtpn*avisitn*sergr1 /
dist=bin link=logit solution or;
   random intercept / subject=subjid type=vc;
   estimate '0.02% vs. Pbo Month 36' trtpn 0 1 -1 trtpn*avisitn 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0  0 0 -1;
```

*estimate '0.02% vs. Pbo Month 36 Low ' trtpn 0 1 -1 trtpn*avisitn 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 -1 trtpn*avisitn*blmymop 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 -1 0;*

*estimate '0.02% vs. Pbo Month 36 High ' trtpn 0 1 -1 trtpn*avisitn 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 -1 trtpn*avisitn*blmymop 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 -1;*

Summary statistics will be presented along with a full data listing by treatment group.

8.3.13. Interaction between Demographic Variables and SER

Tertiary analyses will be performed on differences between select demographic variables (age 6 – 8 years versus 9 – 10 years; baseline SER -0.50 to -3.00 D versus -3.01 to 6.00 D SER; Asian versus non-Asian; dark irides versus light irides, region (U.S. versus E.U.); female versus male) and change from baseline in SER at Month 12, Month 24, and Month 36. The analysis method will be the same as the primary or secondary efficacy analysis as described in 8.1.1 and 8.2.1 respectively above , except for the addition of the particular demographic variable being analyzed and an associated treatment interaction term. Testing of the difference in demographic variable and the demographic variable by treatment interaction term will be provided. The tertiary analysis will be performed using the mITT set only.

For the purpose of analysis of irides, light irides will consist of Grade 1 – Grade 3 iris colors while dark irides consist of Grade 4 and Grade 5 iris colors. Similarly, for the analysis of race, Asian will be defined as Japanese, East Asian, and South Asian. Non-Asian races will consist of all other non-missing races.

Summary statistics will be presented along with a full data listing by treatment group.

8.3.14. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.02% Versus Vehicle) Difference in the Mean Change from Baseline in Crystalline Lens Thickness at the Month 36 visit

A tertiary analysis will be performed on the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.02% versus vehicle) difference in the mean change from baseline in crystalline lens thickness at the Month 36 visit. The analysis method will be the same as the secondary efficacy analysis as described in 8.2.1 above. The tertiary analysis will be performed using the mITT and ITT sets.

Summary statistics will be presented along with a full data listing by treatment group.

8.3.15. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.01% Versus Vehicle) Difference in the Mean Change from Baseline in Crystalline Lens Thickness at the Month 36 visit

A tertiary analysis will be performed on the between-treatment group (Atropine Sulfate Ophthalmic Solution, 0.01% versus vehicle) difference in the mean change from baseline in crystalline lens thickness at the Month 36 visit. The analysis method will be the same as the secondary efficacy analysis as described in 8.2.1 above. The tertiary analysis will be performed using the mITT and ITT sets.

Summary statistics will be presented along with a full data listing by treatment group.

8.3.16. Rebound Assessment Based on the Change from Stage 2 Baseline (Month 36) at Months 42 and 48

The change from baseline from Stage 2 baseline (Month 36) to the Moth 42 and Month 48 visits will be summarized using descriptive statistics. Summaries will be provided for active treatment Stage 1 subjects who received the same or lower dose, including placebo, Summaries will be provided for Stage 1 and Stage 2 treatment combinations listed:

- Atropine Sulfate Ophthalmic Solution, 0.02% -> Atropine Sulfate Ophthalmic Solution, 0.02%
- Atropine Sulfate Ophthalmic Solution, 0.02% -> Atropine Sulfate Ophthalmic Solution, 0.01%
- Atropine Sulfate Ophthalmic Solution, 0.02% -> Vehicle
- Atropine Sulfate Ophthalmic Solution, 0.01% -> Atropine Sulfate Ophthalmic Solution, 0.01%
- Atropine Sulfate Ophthalmic Solution, 0.01% -> Vehicle

8.3.17. Rebound Assessment Based on the Responders at Months 42 and 48

For subject on active treatment who were responders (subjects' eyes who show less than 0.5 D myopia progression (SER) from baseline at the Month 36 visit) in Stage 1, their progression from Stage 1 baseline at Month 42 and Month 48 will by summarize using count and percentage.

Summaries will be provided for Stage 1 and Stage 2 treatment combinations listed:

- Atropine Sulfate Ophthalmic Solution, 0.02% -> Atropine Sulfate Ophthalmic Solution, 0.02%
- Atropine Sulfate Ophthalmic Solution, 0.02% -> Atropine Sulfate Ophthalmic Solution, 0.01%
- Atropine Sulfate Ophthalmic Solution, 0.02% -> Vehicle
- Atropine Sulfate Ophthalmic Solution, 0.01% -> Atropine Sulfate Ophthalmic Solution, 0.01%
- Atropine Sulfate Ophthalmic Solution, 0.01% -> Vehicle

8.4. Exploratory Efficacy Analyses

For all Stage 2 exploratory analyses, summary statistics will be provided based on the Stage 1 to Stage 2 treatment description. Analyses table will only include the groups presented in the analyses. The eight treatment groups for these tables will include:

- Atropine Sulfate Ophthalmic Solution, 0.02% -> Atropine Sulfate Ophthalmic Solution, 0.02%
- Atropine Sulfate Ophthalmic Solution, 0.02% -> Atropine Sulfate Ophthalmic Solution, 0.01%
- Atropine Sulfate Ophthalmic Solution, 0.02% -> Vehicle
- Atropine Sulfate Ophthalmic Solution, 0.01% -> Atropine Sulfate Ophthalmic Solution, 0.02%
- Atropine Sulfate Ophthalmic Solution, 0.01% -> Atropine Sulfate Ophthalmic Solution, 0.01%
- Atropine Sulfate Ophthalmic Solution, 0.01% -> Vehicle
- Vehicle -> Atropine Sulfate Ophthalmic Solution, 0.02%
- Vehicle -> Atropine Sulfate Ophthalmic Solution, 0.01%

8.4.1. Between-treatment Group (Atropine Sulfate Ophthalmic Solution, 0.02% versus Vehicle and Atropine Sulfate Ophthalmic Solution, 0.01% versus Vehicle) Difference in the Proportion of

Subjects' Eyes with Higher Myopia (SER <= -3.00) who Show less than 0.75 D Myopia Progression (SER) From Baseline at the Month 36 Visit

An exploratory analysis will be performed on difference in the proportion of subjects' eyes who show less than 0.75 D myopia progression (SER) from baseline at the Month 36 visit. The analysis method will be the same as the primary efficacy analysis as described in 8.1.1 above.

Summary statistics will be presented by treatment group.

8.4.2. Between-treatment Group Difference in the Mean Change from Study Baseline in SER at the Month 48 Visit.

The analysis will be performed using the same methods as in 8.2.1 above. Only the four indicated arms being test will be included in the analysis model. The analysis will be performed using the mITT analysis set. The following treatment comparisons will be made:

- Atropine Sulfate Ophthalmic Solution, 0.02% -> Atropine Sulfate Ophthalmic Solution, 0.02% vs. Atropine Sulfate Ophthalmic Solution, 0.02% -> Vehicle
- Atropine Sulfate Ophthalmic Solution, 0.01% -> Atropine Sulfate Ophthalmic Solution, 0.01% vs. Atropine Sulfate Ophthalmic Solution, 0.01% -> Vehicle

Summary statistics and figure will be presented along with a full data listing for all treatment groups.

8.4.3. Between-treatment Group Difference in the Mean Change from Stage 2 Baseline (Month 36) in SER at the Month 48 Visit.

The analysis will be performed using the same methods as in 8.2.1 above.

Only the four indicated arms being test will be included in the analysis model. The analysis will be performed using the mITT analysis set. The following treatment comparisons will be made:

- Atropine Sulfate Ophthalmic Solution, 0.02% -> Atropine Sulfate Ophthalmic Solution, 0.02% vs. Atropine Sulfate Ophthalmic Solution, 0.02% -> Vehicle
- Atropine Sulfate Ophthalmic Solution, 0.01% -> Atropine Sulfate Ophthalmic Solution, 0.01% vs. Atropine Sulfate Ophthalmic Solution, 0.01% -> Vehicle

Summary statistics and figure will be presented along with a full data listing for all treatment groups.

8.4.4. Other Stage 2 Exploratory Endpoints

For endpoints described in Sections 8.3.1 through 8.3.15, Summary statistics and listings will be provided for Stage 2 using the treatment groups described in 8.4 above.

9. Safety

The population used for safety analyses will be the Safety Set (SS). Safety will be assessed on the basis of ophthalmic safety assessments (BCVA, photopic pupil size, slit-lamp examination (SLE), dilated fundus examination, and tonometry), HR, and adverse events (AE). Safety Tables will be provided separately for each stage of the study.

9.1. Extent of Exposure

Duration of exposure will be summarized using descriptive statistics by treatment group for each stage. The duration of exposure will also be categorized (<6, 6-<12, 12-<18, 18-<24, 24-<30, 30-<36, ≥36 months for Stage 1; <3, 3-<6, 6-<9, 9-<12, ≥12 months for Stage 2), and tabulated by treatment group. Duration of exposure (months) will be calculated as ((Date of Last Dose – Date of First Dose) +1)/30.4375). If date of last dose is unknown, then the date of last clinical visit will be used.

9.2. Treatment Compliance

Subjects are expected to take 1 drop of study medication per eye, once per day.

Treatment compliance for Stage 1, as a percentage, will be calculated as compliance (%) = (number of ampules used as determined in Interactive Response Technology) / ((Date of Last Dose of Stage 1 – Date of First Dose of Stage 1) +1)) x 100. The number of actual doses withheld will be recorded in the eCRF.

Starting on the day of the Month 36 visit, subjects were switch to an electronic dosing diary. Each eye's dosing is collected independently, based on whether eye drops were applied or not for each eye. Any missing dosing information between Month 36 visit and last reported dose will be considered as missed dose(s). Treatment compliance for Stage 2, as a percentage, will be calculated as compliance (%) = (sum of number of reported doses / ((Date of Last Dose of Stage 2 – Date of First Dose of Stage 2) + 1)) x 100.

Subjects will be considered compliant overall for study medication if the compliance is ≥80%. Descriptive statistics (number of subjects, mean, SD, minimum, median, and maximum) for number of ampules used (Stage 1), number of doses received (Stage 2) and treatment compliance will be summarized by treatment group for Safety Set by actual treatment and stage and for the ITT Set, the mITT Set, the PPS, and the mPPS by randomized treatment for each stage.

Given the duration a subject is enrolled in the study, it is possible for the subject to begin self-dosing instead of parental dosing. All subjects will be asked if this occurred and when the change occurred. The number and percentage of subject switching to self-dosing during the course of the study will be summarized by Stage 1 treatment group and overall.

9.3. Adverse Events

The analysis of AEs will be based on the concept of treatment-emergent AEs (TEAEs). An adverse event is any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug-related.

Treatment-emergent adverse events (TEAEs) of Stage 1 are defined as any new or worsening of existing adverse events that occur or worsen between start (or increase in intensity on or after the first dose date

of Stage 1 treatment on day 1) and the last dose date of Stage 1. TEAEs of Stage 2 are defined as any AE that occurs or worsens between the first dose date of Stage 2 and the last dose date of Stage 2.

The first dose date for Stage 1 is defined as the first dose of study medication received after randomization in Stage 1. The first dose date for Stage 2 is defined as the first dose of study medication received after the Stage 1 last dose date and subject is re-randomized. All adverse events (AEs) will be coded using the MedDRA version 20.1 or higher. The following listings of AEs will be provided by Stage and subjects:

- All AEs,
- Serious adverse events (SAEs) Serious ocular and non-ocular AEs, respectively
- All deaths
- TEAEs (overall, ocular, non-ocular, respectively) leading to study withdrawal
- TEAEs (overall, ocular, non-ocular, respectively) leading to study drug discontinuation
- Severe AEs
- Study drug related AEs
- Study drug related SAEs

Treatment-emergent adverse events will be included in summary tables by treatment received for each stage. Ocular TEAEs will be summarized separately from all other TEAEs. An overall summary table of TEAEs for each stage will be produced for the following categories:

- Any Ocular TEAE
- Severe Ocular TEAEs
- Study drug-related Ocular TEAEs
- Serious Ocular TEAEs
- Study drug-related Serious Ocular TEAEs
- Ocular TEAEs leading to study discontinuation
- Ocular TEAEs leading to death
- Any Non-Ocular TEAE
- Severe Non-Ocular TEAEs
- Study drug-related Non-Ocular TEAEs
- Serious Non-Ocular TEAEs
- Study drug-related Serious Non-Ocular TEAEs
- Non-Ocular TEAEs leading to study discontinuation
- Non-Ocular TEAEs leading to death

All TEAEs will be classified by System Organ Class (SOC) and Preferred Term (PT). Frequency count of TEAEs, the number of unique subjects experiencing a TEAE, percentage of unique subjects experiencing a TEAE, and total number of events will be tabulated by treatment and Stage for ocular and other TEAEs separately. For the number of unique subjects reporting, if a subject reported more than one TEAE that was coded to the same SOC or PT, the subject will be counted only once for that specific SOC or PT.

The following summaries of TEAEs will also be provided:

- TEAEs by SOC and PT
- Ocular TEAEs by SOC and PT
- Non-Ocular TEAEs by SOC and PT

- TEAEs by SOC, PT, and maximum severity
- Ocular TEAEs by SOC, PT, and maximum severity
- Non-Ocular TEAEs by SOC, PT, and maximum severity
- TEAEs by SOC, PT, and maximum relationship
- Ocular TEAEs by SOC, PT, and maximum relationship
- Non-Ocular TEAEs by SOC, PT, and maximum relationship
- Treatment-related TEAEs by SOC and PT
- Ocular Treatment-related TEAEs by SOC and PT
- Non-Ocular Treatment-related TEAEs by SOC and PT
- Serious TEAEs by SOC and PT
- Serious Ocular TEAEs by SOC and PT
- Serious Non-Ocular TEAEs by SOC and PT
- Serious treatment-related TEAEs by SOC and PT
- Serious Ocular treatment-related TEAEs by SOC and PT
- Serious Non-Ocular treatment-related TEAEs by SOC and PT
- TEAEs leading to study withdrawal by SOC and PT
- Ocular TEAEs leading to study withdrawal by SOC and PT
- Non-Ocular TEAEs leading to study withdrawal by SOC and PT
- TEAEs leading to study drug discontinuation by SOC and PT
- Ocular TEAEs leading to study drug discontinuation by SOC and PT
- Non-Ocular TEAEs leading to study drug discontinuation by SOC and PT
- TEAEs leading to death by SOC and PT
- Ocular TEAEs leading to death by SOC and PT
- Non-Ocular TEAEs leading to death by SOC and PT
- TEAEs associated with antimuscarinic function
- Ocular TEAEs associated with antimuscarinic function
- Non-Ocular TEAEs associated with antimuscarinic function
- TEAEs by SOC, PT and Sex
- Ocular TEAEs by SOC, PT and Sex
- Non-Ocular TEAEs by SOC, PT and Sex
- TEAEs by SOC, PT and Race
- Ocular TEAEs by SOC, PT and Race
- Non-Ocular TEAEs by SOC, PT and Race
- TEAEs by SOC, PT and Age
- Ocular TEAEs by SOC, PT and Age
- Non-Ocular TEAEs by SOC, PT and Age

For TEAEs presented by relationship to study treatment, the strongest relationship to study treatment(s) during the clinical trial will be presented for each subject if coded to the same SOC or PT. For TEAEs presented by severity, the worst severity during the clinical trial will be presented for each subject if coded to the same SOC or PT. If either relationship or severity is missing, then the strongest relationship (related) or worst severity (life-threatening) will be assigned. Adverse Events associated with antimuscarinic function are defined in Table 3.

Table 3: Adverse Events Associated with Antimuscarinic Function

Classification	Preferred Term
Ophthalmic	Photophobia
	Dyschromatopsia
	Night blindness
	Angle closure glaucoma
	Lacrimation decreased
Non-Ophthalmic	Blood pressure increased
	Heart rate increased
	Dry skin
	Dry mouth
	Dry throat
	Restlessness
	Irritability
	Delirium
	Flushing
	Seizure
	Epilepsy
	Urinary retention
	Obstruction gastric
	Bronchial secretion retention
	Arrhythmia

9.4. Heart Rate, Weight, and Height

Heart rate is collected at Baseline and the Month 6, 12, 18, 24, 30, 36, 42, and 48 visits. Weight and height are collected at Baseline and the Month 12, 24, 36, and 48 visits.

Observed values at each visit and changes from study Baseline to each post-baseline visit will be summarized by stage, visit and treatment group using descriptive statistics.

Heart rate will be provided in subject data listings.

9.5. Monocular Best-Corrected Visual Acuity (BCVA)

Monocular Best-Corrected Visual Acuity (BCVA) is performed at Baseline and the Month 6, 12, 18, 24, 30, 36, 42, and 48 visits. BCVA will be provided as LogMar BCVA for both distance and near for each eye.

Observed values at each visit and changes from Baseline to each post-baseline visit will be summarized by stage, visit and treatment group using descriptive statistics. For Stage 2, the Stage 2 baseline (Month 36) will be used for the change from baseline calculation. Changes that warranted a new prescription will also be identified.

Monocular Best-Corrected Visual Acuity will be provided in subject data listings.

9.6. Photopic Pupil Size

Photopic pupil size (mm) is collected at Baseline and the Month 6, 12, 18, 24, 30, 36, 42, and 48 visits. Photopic pupil size will be provided for each eye individually.

Observed values at each visit and changes from Baseline to each post-baseline visit will be summarized by stage, visit and treatment group using descriptive statistics. For Stage 2, the Stage 2 baseline (Month 36) will be used for the change from baseline calculation.

Photopic pupil size will be provided in subject data listings.

9.7. Slit Lamp Examination

A slit lamp exam is performed at Baseline and the Month 6, 12, 18, 24, 30, 36, 42, and 48 visits. Assessments of conjunctiva, cornea, anterior chamber, iris, lens, and lids will be provided for each eye individually.

Findings at each visit will be summarized by stage, visit and treatment group using descriptive statistics.

Slit lamp exam results will be provided in subject data listings.

9.8. Dilated Fundus Examination

A dilated fundus examination is performed at Baseline and the Month 12, 24, 36, and 48 visits. Assessments of optic nerve head, macula, peripheral retina, iris, and vitreous will be provided for each eye individually.

Findings at each visit will be summarized by stage, visit and treatment group using descriptive statistics.

Dilated fundus examination results will be provided in subject data listings.

9.9. Intraocular Pressure

Intraocular pressure (mmHg) is measured at Baseline and the Month 6, 12, 18, 24, 30, 36, 42, and 48 visits. Measurement of intraocular pressure will be provided for each eye individually.

Observed values at each visit and changes from Baseline to each post-baseline visit will be summarized by stage, visit and treatment group using descriptive statistics. For Stage 2, the Stage 2 baseline (Month 36) will be used for the change from baseline calculation.

Intraocular pressure measurements will be provided in subject data listings.

10. Quality of Life

10.1. Modified Amblyopia Treatment Index (mATI)

The Amblyopia Treatment Index (ATI) was developed by the Pediatric Eye Disease Investigator Group to measure the impact or burden of amblyopia treatment on the child and the family. The Modified Amblyopia Treatment Index (mATI) consists of 2 questionnaires. One is completed by a Parent/ Guardian while the second is completed by the subject at the Month 42 and Month 48 visits. The questionnaires consist of 16 or 15 questions respectively using a five-point Likert scale for each question.

The questionnaires will be scored to an Overall Score and 3 subscales (Adverse Event, Treatment Compliance, and Social Stigma). Questionnaires with 3 or more missing or not applicable responses will not be scored or analyzed. For questionnaires with 1 or 2 missing or not applicable responses, these responses will be imputed with the average score for all completed items. See Table 4: Modified Amblyopia Treatment Index Scoring for scoring methodology.

Table 4: Modified Amblyopia Treatment Index Scoring

Score	Parent	Child
Overall	Mean of (Items 1*, 2, 3, 4, 5, 6, 7, 8, 9*, 10, 11, 12, 13, 14*, 15, 16)	Mean of (Items 1, 2, 3, 4, 5, 6, 7, 8*, 9, 10, 11, 12, 13*, 14, 15)
Adverse effect subscale	Mean of (Items 2, 3, 4, 7, 8, 9*, 13, 15)	Mean of (Items 2, 3, 4, ~~8~~6, ~~9~~7, 8*, 12, 14)
Treatment compliance subscale	Mean of (Items 1*, 5, 6, 10, 12)	Mean of (Items 1, 5, 9, 11)
Social stigma subscale	Item 11	Item 10

*Reverse scoring applied. Value used in scoring = (6- reported score)

Overall and subscale scores for mATI will be summarized by visit and Stage 2 treatment group using descriptive statistics as both a continuous and categorical variable. Individual item and all scores will be listed.

11. Interim Analyses

In order to determine the efficacy of Atropine Sulfate Ophthalmic Solution in progression of childhood myopia, an analysis will be performed after all subjects complete or withdraw from Stage 1. At that time, on Stage 1 treatment assignments will be unblinded and no analyses or summaries will be provided for Stage 2 results. All study personnel, not including Investigators, site staff, and clinical research associates (CRAs), may be unblinded for Stage 1 at this time.

All analyses will be performed as documented in the SAP. No decisions regarding the study or changes in the study are to be made at that time.

12. Changes from Analysis Planned in Protocol

Not all sites used the same Vertex distance (VD) in mm when measuring refraction with autorefractor. All averaged SER from each participant used in tables and analyses will be normalized to a VD of 0 mm to the corneal plane. The normalization will be applied using

$$SSSSSS_{nnnnnnnnnnnnnnnnnn} = \frac{100}{\frac{100}{SSSSSS} - \frac{VVVV}{10}}$$

where SER is the original SER from CRF.

13. Programming Considerations

All tables, figures, listings (TFLs), and statistical analyses will be generated using SAS for Windows, Release 9.4 (SAS Institute Inc., Cary, NC, USA). Computer-generated table, listing and figure output will adhere to the following specifications.

13.1. General Considerations.

- One SAS program can create several outputs, or a separate SAS program will be created for each output.
- Each output will be stored in a separate file.
- Output files will be delivered in Word format or portable document format pdf.
- Numbering of TFLs will follow ICH E3 guidance

13.2. Table, Listing, and Figure Format

13.2.1. General

- All TFLs will be produced in landscape format on American letter size, unless otherwise specified.
- All TFLs will be produced using the Courier New font, size 8 which is the smallest acceptable point size for the Regulatory Authorities.
- The data displays for all TFLs will have a minimum blank 1-inch margin on all 4 sides.
- Headers and footers for figures will be in Courier New font, size 8 which is the smallest acceptable point size for the Regulatory Authorities.
- Legends will be used for all figures with more than 1 variable, group, or item displayed.
- TFLs will be in black and white (no color), unless otherwise specified
- Specialized text styles, such as bolding, italics, borders, shading, and superscripted and subscripted text, will not be used in the TFLs, unless otherwise specified. On some occasions, superscripts 1, 2, or 3 may be used (see below).
- Only standard keyboard characters will be used in the TFLs. Special characters, such as non-printable control characters, printer-specific, or font-specific characters, will not be used. Hexadecimal-derived characters will be used, where possible, if they are appropriate to help display math symbols (e.g., μ). Certain subscripts and superscripts (e.g., cm^2, Cmax) will be employed on a case-by-case basis.
- Mixed case will be used for all titles, footnotes, column headers, and programmer-supplied formats, as appropriate.

13.2.2. Headers

- All output should have the following header at the top left of each page:
- Vyluma, Inc. Protocol CP-NVK002-0001 (Syneos Health study number 1)

- Draft/Final Run <date>
- All output should have Page n of N at the top or bottom right corner of each page. TFLs are internally paginated in relation to the total length (i.e., the page number should appear sequentially as page n of N, where N is the total number of pages in the table).
- The date output was generated should appear along with the program name as a footer on each page.

13.2.3. Display Titles

- Each TFL are identified by the designation and a numeral. (i.e., Table 14.1.1). ICH E3 numbering is strongly recommended, but sponsor preferences are obtained before final determination. A decimal system (x.y and x.y.z) are used to identify TFLs with related contents. The title is centered. The analysis set are identified on the line immediately following the title. The title and table designation are single-spaced. A solid line spanning the margins will separate the display titles from the

Table x.y.z
First Line of Title
Second Line of Title if Needed
(ITT Analysis Set)

13.2.4. Column Headers

- Column headings are displayed immediately below the solid line described above in initial upper-case characters.
- In the case of efficacy tables, the variable (or characteristic) column will be on the far left followed by the treatment group columns and total column (if applicable). P-values may be presented under the total column or in separate p-value column (if applicable). Within-treatment comparisons may have p-values presented in a row beneath the summary statistics for that treatment.
- For numeric variables, include “unit” in column or row heading when appropriate.
- Analysis set sizes will be presented for each treatment group in the column heading as (N=xx) (or in the row headings, if applicable). This is distinct from the ‘n’ used for the descriptive statistics representing the number of subjects in the analysis set.

- The order of treatment groups in the tables and listings will be Placebo first then Atropine Sulfate Ophthalmic Solution, 0.01%, and Atropine Sulfate Ophthalmic Solution, 0.02% followed by a total column (if applicable).

13.2.5. Body of the Data Display

13.2.5.1. *General Conventions*

Data in columns of a table or listing are formatted as follows:

- Alphanumeric values are left-justified;
- Whole numbers (e.g., counts) are right-justified; and

- Numbers containing fractional portions are decimal aligned.

13.2.5.2. *Table Conventions*

- Units will be included where available

- If the categories of a parameter are ordered, then all categories between the maximum and minimum category are presented in the table, even if n=0 for all treatment groups in a given category that is between the minimum and maximum level for that parameter. For example, the frequency distribution for symptom severity would appear as:

Severity Rating	N
severe	0
moderate	8
mild	3

Where percentages are presented in these tables, zero percentages will not be presented and so counts of 0 will be presented as 0 and not as 0 (0%).

- If the categories are not ordered (e.g., Medical History, Reasons for Discontinuation from the Study, etc.), then only those categories for which there is at least 1 subject represented in 1 or more groups are included.

- An Unknown or Missing category are added to each parameter for which information is not available for 1 or more subjects.

- Unless otherwise specified, the estimated mean and median for a set of values are printed out to 1 more significant digit than the original values, and standard deviations are printed out to 2 more significant digits than the original values. The minimum and maximum should report the same significant digits as the original values. For example, for systolic blood pressure:

N	XX
Mean	XXX.X
Std Dev	X.XX
Median	XXX.X
Minimum	XXX
Maximum	XXX

- P-values are output in the format: “0.xxx”, where xxx is the value rounded to 3 decimal places. Every p-value less than 0.001 will be presented as <0.001. If the p-value are less than 0.0001, then present as <0.0001. If the p-value is returned as >0.999, then present as >0.999

- Percentage values are printed to one decimal place, in parentheses with no spaces, one space after the count (e.g., 7 (12.8%), 13 (5.4%)). Pre-determine how to display values that round down to 0.0. A common convention is to display as '<0.1', or as appropriate with additional decimal places. Unless otherwise noted, for all percentages, the number of subjects in the analysis set for the treatment group who have an observation will be the denominator. Percentages after zero

counts should not be displayed and percentages equating to 100% are presented as 100%, without decimal places.

- Tabular display of data for medical history, prior/concomitant medications, and all tabular displays of adverse event data are presented by the body system, treatment class, or SOC with the highest occurrence in the active treatment group in decreasing order, assuming all terms are coded. Within the body system, drug class and SOC, medical history (by preferred term), drugs (by ATC1 code), and adverse events (by preferred term) are displayed in decreasing order. If incidence for more than 1 term is identical, they should then be sorted alphabetically. Missing descriptive statistics or p-values which cannot be estimated are reported as "-".

- The percentage of subjects is normally calculated as a proportion of the number of subjects assessed in the relevant treatment group (or overall) for the analysis set presented. However, careful consideration is required in many instances due to the complicated nature of selecting the denominator, usually the appropriate number of subjects exposed. Describe details of this in footnotes or programming notes.

- For categorical summaries (number and percentage of subjects) where a subject can be included in more than one category, describe in a footnote or programming note if the subject is included in the summary statistics for all relevant categories or just 1 category and the criteria for selecting the criteria.

- Where a category with a subheading (such as system organ class) has to be split over more than one page, output the subheading followed by "(cont)" at the top of each subsequent page. The overall summary statistics for the subheading should only be output on the first relevant page.

13.2.5.3. *Listing Conventions*

- Listings will be sorted for presentation in order of treatment groups as above, subject number, visit/collection day, and visit/collection time.

- Missing data are represented on subject listings as either a hyphen ("-") with a corresponding footnote ("- = unknown or not evaluated"), or as "N/A", with the footnote "N/A = not applicable", whichever is appropriate.

- Dates are printed in SAS DATE9.format ("ddMMMyyyy": 01JUL2000). Missing portions of dates are represented on subject listings as dashes (--JUL2000). Dates that are missing because they are not applicable for the subject are output as "N/A", unless otherwise specified.

- All observed time values are to be presented using a 24-hour clock HH:MM or HH:MM:SS format (e.g., 11:26:45, or 11:26). Time will only be reported if it was measured as part of the study.

- Units will be included where available

13.2.5.4. *Figure Conventions*

- Unless otherwise specified, for all figures, study visits will be displayed on the X-axis and endpoint (e.g., treatment mean change from Baseline) values will be displayed on the Y-axis.

13.2.6. Footnotes

- A solid line spanning the margins will separate the body of the data display from the footnotes.
- All footnotes will be left justified with single-line spacing immediately below the solid line underneath the data display.
- Footnotes should always begin with “Note:” if an informational footnote, or 1, 2, 3, etc. if a reference footnote. Each new footnote should start on a new line, where possible.
- Subject specific footnotes are avoided, where possible.
- Footnotes will be used sparingly and add value to the table, figure, or listing. If more than six lines of footnotes are planned, then a cover page is strongly recommended to be used to display footnotes, and only those essential to comprehension of the data will be repeated on each page.
- Analysis population definition will be provided in the footnote of each table.
- The last line of the footnote section will be a standard source line that indicates the name of the program used to produce the data display, date the program was run, and the listing source (i.e., ‘Program : myprogram.sas Listing source: 16.x.y.z’).

14. Quality Control

SAS programs are developed to produce output such as analysis data sets, summary tables, data listings, figures, or statistical analyses. An overview of the development of programs is detailed in Syneos Health SOP Developing Statistical Programs (3907).

Syneos Health SOPs Developing Statistical Programs (3907) and Conducting the Transfer of Biostatistical Deliverables (3908) describes the quality control procedures that are performed for all SAS programs and output. Quality control is defined here as the operational techniques and activities undertaken to verify that the SAS programs produce the output by checking for their logic, efficiency and commenting and by review of the produced output."

15. References

Fannin TE, Grosvenor T. Clinical Optics. 1st edition. Butterworth-Heinemann. 1987. Equation 3.16, page 71.

16. Index of Tables

Header	Table Number	Name	Analysis Set
14.		Tables, Figures, and Graphs Referred to but not Included in the Text	
14.1		Demographic Data Summary Tables	
14.1.1		Subject Disposition	
	14.1.1.1.1	Number of Subjects Enrolled and Study Termination – Stage 1	Stage 1 Enrolled Set
	14.1.1.1.2	Number of Subjects Enrolled and Study Termination – Stage 2	Stage 2 Enrolled Set
14.1.2		Protocol Deviations	
	14.1.2.1	Major Protocol Deviations	Intent-to-Treat Set
14.1.3		Demographic and Baseline Characteristics	
14.1.3.1		Subject Demographic and Baseline Characteristics	
	14.1.3.1.1.1	Subject Demographic and Baseline Characteristics – Stage 1 Subjects	Stage 1 Safety Set
	14.1.3.1.1.2	Subject Demographic and Baseline Characteristics – Stage 2 Subjects	Stage 2 Safety Set
	14.1.3.1.2.1	Subject Demographic and Baseline Characteristics – Stage 1 Subjects	Stage 1 Intent-to-Treat Set
	14.1.3.1.2.2	Subject Demographic and Baseline Characteristics – Stage 2 Subjects	Stage 2 Intent-to-Treat Set
	14.1.3.1.3.1	Subject Demographic and Baseline Characteristics – Stage 1 Subjects	Stage 1 Modified Intent-to-Treat Set
	14.1.3.1.3.2	Subject Demographic and Baseline Characteristics – Stage 2 Subjects	Stage 2 Modified Intent-to-Treat Set
	14.1.3.1.4.1	Subject Demographic and Baseline Characteristics – Stage 1 Subjects	Stage 1 Per Protocol Set
	14.1.3.1.4.2	Subject Demographic and Baseline Characteristics – Stage 2 Subjects	Stage 2 Per Protocol Set
	14.1.3.1.5.1	Subject Demographic and Baseline Characteristics – Stage 1 Subjects	Stage 1 Modified Per Protocol Set
	14.1.3.1.5.2	Subject Demographic and Baseline Characteristics – Stage 2 Subjects	Stage 2 Modified Per Protocol Set
14.1.3.2		Baseline Disease Characteristics	
	14.1.3.2.1.1	Baseline Disease Characteristics – Stage 1 Subjects	Stage 1 Safety Set
	14.1.3.2.1.2	Baseline Disease Characteristics – Stage 2 Subjects	Stage 2 Safety Set
	14.1.3.2.2.1	Baseline Disease Characteristics – Stage 1 Subjects	Stage 1 Intent-to-Treat Set
	14.1.3.2.2.2	Baseline Disease Characteristics – Stage 2 Subjects	Stage 2 Intent-to-Treat Set
	14.1.3.2.3.1	Baseline Disease Characteristics – Stage 1 Subjects	Stage 1 Modified Intent-to-Treat Set
	14.1.3.2.3.2	Baseline Disease Characteristics – Stage 2 Subjects	Stage 2 Modified Intent-to-Treat Set
	14.1.3.2.4.1	Baseline Disease Characteristics – Stage 1 Subjects	Stage 1 Per Protocol Set

Header	Table Number	Name	Analysis Set
	14.1.3.2.4.2	Baseline Disease Characteristics – Stage 2 Subjects	Stage 2 Per Protocol Set
	14.1.3.2.5.1	Baseline Disease Characteristics – Stage 1 Subjects	Stage 1 Modified Per Protocol Set
	14.1.3.2.5.2	Baseline Disease Characteristics – Stage 2 Subjects	Stage 2 Modified Per Protocol Set
14.1.3.3		Medical History	
	14.1.3.3.1	Ocular Medical History by System Organ Class and Preferred Term	Safety Set
	14.1.3.3.2	Medical History by System Organ Class and Preferred Term	Safety Set
14.1.4		Medications	
	14.1.4.1	Prior Medications	Safety Set
	14.1.4.2.1	Concomitant Medications – Stage 1	Stage 1 Safety Set
	14.1.4.2.2	Concomitant Medications – Stage 2	Stage 2 Safety Set
14.1.5.1		Treatment Compliance	
	14.1.5.1.1.1	Treatment Compliance – Stage 1	Stage 1 Safety Set
	14.1.5.1.1.2	Treatment Compliance – Stage 2	Stage 2 Safety Set
	14.1.5.1.2.1	Treatment Compliance – Stage 1	Stage 1 Intent-to-Treat Set
	14.1.5.1.2.2	Treatment Compliance – Stage 2	Stage 2 Intent-to-Treat Set
	14.1.5.1.3.1	Treatment Compliance – Stage 1	Stage 1 Modified Intent-to-Treat Set
	14.1.5.1.3.2	Treatment Compliance – Stage 2	Stage 2 Modified Intent-to-Treat Set
	14.1.5.1.4.1	Treatment Compliance – Stage 1	Stage 1 Per Protocol Set
	14.1.5.1.4.2	Treatment Compliance – Stage 2	Stage 2 Per Protocol Set
	14.1.5.1.5.1	Treatment Compliance – Stage 1	Stage 1 Modified Per Protocol Set
	14.1.5.1.5.2	Treatment Compliance – Stage 2	Stage 2 Modified Per Protocol Set
14.1.5.2		Extent of Exposure	
	14.1.5.2.1.1	Extent of Exposure – Stage 1	Stage 1 Safety Set
	14.1.5.2.1.2	Extent of Exposure – Stage 2	Stage 2 Safety Set
	14.1.5.2.2.1	Extent of Exposure – Stage 1	Stage 1 Intent-to-Treat Set
	14.1.5.2.2.2	Extent of Exposure – Stage 2	Stage 2 Intent-to-Treat Set
	14.1.5.2.3.1	Extent of Exposure – Stage 1	Stage 1 Modified Intent-to-Treat Set
	14.1.5.2.3.2	Extent of Exposure – Stage 2	Stage 2 Modified Intent-to-Treat Set
	14.1.5.2.4.1	Extent of Exposure – Stage 1	Stage 1 Per Protocol Set
	14.1.5.2.4.2	Extent of Exposure - Stage 2	Stage 2 Per Protocol Set
	14.1.5.2.5.1	Extent of Exposure – Stage 1	Stage 1 Modified Per Protocol Set

Header	Table Number	Name	Analysis Set
	14.1.5.2.5.2	Extent of Exposure - Stage 2	Stage 2 Modified Per Protocol Set
14.2		Efficacy Data Summary Figures and Tables	
14.2.1		Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline	
	14.2.1.1.1	Analysis of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit Mixed Effects Model	Stage 1 Modified Intent-to-Treat Set
	14.2.1.2.1	Analysis of the Composite Proportion of Subjects who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit Supportive Analysis	Stage 1 Modified Intent-to-Treat Set
	14.2.1.2.2	Analysis of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit Sensitivity Analysis	Stage 1 Intent-to-Treat Set
	14.2.1.2.4	Analysis of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit Sensitivity Analysis	Stage 1 Modified Per Protocol Set
	14.2.1.2.6	Analysis of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit Sensitivity Analysis	Stage 1 Per Protocol Set
	14.2.1.3	Analysis of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 Tipping Point Analysis	Stage 1 Modified Intent-to-Treat Set
	14.2.1.4.1	Analysis of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit On-Treatment Analysis	Stage 1 Modified Intent-to-Treat Set

Header	Table Number	Name	Analysis Set
	14.2.1.4.2	Analysis of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit On-Treatment Analysis	Stage 1 Intent-to-Treat Set
	14.2.1.5.1	Analysis of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit (6-8 years old vs. 9-10 years old) Mixed Effect Model	Stage 1 Modified Intent-to-Treat Set
	14.2.1.5.2	Summary of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit (6-8 years old vs. 9-10 years old)	Stage 1 Intent-to-Treat Set
	14.2.1.6.1	Analysis of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit (Baseline SER -0.50 to -3.00 D versus -3.01 to -6.00 D) Mixed Effect Model	Stage 1 Modified Intent-to-Treat Set
	14.2.1.6.2	Summary of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit (Baseline SER -0.50 to -3.00 D versus -3.01 to -6.00 D)	Stage 1 Intent-to-Treat Set
	14.2.1.7.1	Analysis of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit (Asian vs. Non-Asian) Mixed Effect Model	Stage 1 Modified Intent-to-Treat Set
	14.2.1.7.2	Summary of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit (Asian vs. Non-Asian)	Stage 1 Intent-to-Treat Set

Header	Table Number	Name	Analysis Set
	14.2.1.8.1	Analysis of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit (Dark Irides vs. Light Irides) Mixed Effect Model	Stage 1 Modified Intent-to-Treat Set
	14.2.1.8.2	Summary of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit (Dark Irides vs. Light Irides)	Stage 1 Intent-to-Treat Set
	14.2.1.9.1	Analysis of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit (U.S. vs, E.U.) Mixed Effect Model	Stage 1 Modified Intent-to-Treat Set
	14.2.1.9.2	Summary of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit (U.S. vs, E.U.)	Stage 1 Intent-to-Treat Set
	14.2.1.10.1	Analysis of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit (Female vs. Male.) Mixed Effect Model	Stage 1 Modified Intent-to-Treat Set
	14.2.1.10.2	Summary of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit (Female vs. Male)	Stage 1 Intent-to-Treat Set
14.2.2		Secondary Efficacy Parameters	
14.2.2.1		Change from Baseline in Normalized SER	
	14.2.2.1.1	Analysis of the Change from Baseline in Normalized SER (D) in Stage 1 by Treatment Group and Visit Mixed Effect Model	Stage 1 Modified Intent-to-Treat Set
	14.2.2.1.4	Analysis of the Change from Baseline in Normalized SER (D) in Stage 1 by Treatment Group and Visit Mixed Effect Model	Stage 1 Intent-to-Treat Set

Header	Table Number	Name	Analysis Set
	14.2.2.1.7	Summary of the Change from Study Baseline in Normalized SER (D) by Stage, Treatment Group and Visit	Modified Intent-to-Treat Set
	14.2.2.1.8	Summary of the Change from Study Baseline in Normalized SER (D) by Stage, Treatment Group and Visit	Intent-to-Treat Set
14.2.2.2		Change from Baseline in Axial Length at Month 36	
	14.2.2.2.1	Analysis of the Change from Baseline in Axial Length (mm) in Stage 1 by Treatment Group and Visit Mixed Effect Model	Stage 1 Modified Intent-to-Treat Set
	14.2.2.2.4	Analysis of the Change from Baseline in Axial Length (mm) in Stage 1 by Treatment Group and Visit Mixed Effect Model	Stage 1 Intent-to-Treat Set
14.2.3		Tertiary Efficacy Parameters	
14.2.3.1		Proportion of Subjects' Eyes who Show less than 0.75 D Myopia Progression (Normalized SER) from Baseline	
	14.2.3.1.1	Analysis of the Proportion of Subjects' Eyes who Show less than 0.75 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit Mixed Effects Model	Stage 1 Modified Intent-to-Treat Set
	14.2.3.1.3	Analysis of the Proportion of Subjects' Eyes who Show less than 0.75 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit Mixed Effects Model	Stage 1 Intent-to-Treat Set
14.2.3.2		Time to Change in Myopia of -0.75 D Normalized SER	
	14.2.3.2.1	Analysis of Time to Change from Baseline in Myopia Progression of -0.75 D Normalized SER in Stage 1 by Treatment Group Cox Proportional Hazards Regression	Stage 1 Modified Intent-to-Treat Set
	14.2.3.2.3	Analysis of Time to Change from Baseline in Myopia Progression of -0.75 D Normalized SER in Stage 1 by Treatment Group Cox Proportional Hazards Regression	Stage 1 Intent-to-Treat Set
14.2.3.3		New Prescriptions Given After the Start of Treatment due to Progression, at Month 36	
	14.2.3.3.1	Analysis of the New Prescriptions Given After the Start of Treatment due to Progression, at Month 36 Cochran-Mantel-Haenszel Test	Stage 1 Modified Intent-to-Treat Set

Header	Table Number	Name	Analysis Set
	14.2.3.3.2	Analysis of the New Prescriptions Given After the Start of Treatment due to Progression, at Month 36 Cochran-Mantel-Haenszel Test	Stage 1 Intent-to-Treat Set
14.2.3.4		Subjects who Progressed to High Myopia (Normalized SER -6.00 D or more myopic) at Month 36	
	14.2.3.4.1	Analysis of the Proportion of Subjects who Progressed to High Myopia (Normalized SER -6.00 D or more myopic) at Month 36 by Baseline Myopia Mixed Effects Model	Stage 1 Modified Intent-to-Treat Set
	14.2.3.4.2	Analysis of the Proportion of Subjects who Progressed to High Myopia (Normalized SER -6.00 D or more myopic) at Month 36 by Baseline Myopia Mixed Effects Model	Stage 1 Intent-to-Treat Set
14.2.3.5		Interaction between Demographic Variables and Normalized SER	
	14.2.3.5.1.1	Analysis of the Change from Baseline in Normalized SER (D) in Stage 1 by Treatment Group and Visit (6-8 years old vs. 9-10 years old) Mixed Effect Model	Stage 1 Modified Intent-to-Treat Set
	14.2.3.5.1.2	Summary of the Change from Baseline in Normalized SER (D) in Stage 1 by Treatment Group and Visit (6-8 years old vs. 9-10 years old)	Stage 1 Intent-to-Treat Set
	14.2.3.5.2.1	Analysis of the Change from Baseline in Normalized SER (D) in Stage 1 by Treatment Group and Visit (Baseline SER -0.50 to -3.00 D versus -3.01 to -6.00 D D) Mixed Effect Model	Stage 1 Modified Intent-to-Treat Set
	14.2.3.5.2.2	Summary of the Change from Baseline in Normalized SER (D) in Stage 1 by Treatment Group and Visit (Baseline SER -0.50 to -3.00 D versus -3.01 to -6.00 D D)	Stage 1 Intent-to-Treat Set

Header	Table Number	Name	Analysis Set
	14.2.3.5.3.1	Analysis of the Change from Baseline in Normalized SER (D) in Stage 1 by Treatment Group and Visit (Asian vs. Non-Asian) Mixed Effect Model	Stage 1 Modified Intent-to-Treat Set
	14.2.3.5.3.2	Summary of the Change from Baseline in Normalized SER (D) in Stage 1 by Treatment Group and Visit (Asian vs. Non-Asian)	Stage 1 Intent-to-Treat Set
	14.2.3.5.4.1	Analysis of the Change from Baseline in Normalized SER (D) in Stage 1 by Treatment Group and Visit (Dark Irides vs. Light Irides) Mixed Effect Model	Stage 1 Modified Intent-to-Treat Set
	14.2.3.5.4.2	Summary of the Change from Baseline in Normalized SER (D) in Stage 1 by Treatment Group and Visit (Dark Irides vs. Light Irides)	Stage 1 Intent-to-Treat Set
	14.2.3.5.5.1	Analysis of the Change from Baseline in Normalized SER (D) in Stage 1 by Treatment Group and Visit (U.S. vs, E.U.) Mixed Effect Model	Stage 1 Modified Intent-to-Treat Set
	14.2.3.5.5.2	Summary of the Change from Baseline in Normalized SER (D) in Stage 1 by Treatment Group and Visit (U.S. vs, E.U.)	Stage 1 Intent-to-Treat Set
	14.2.3.5.6.1	Analysis of the Change from Baseline in Normalized SER (D) in Stage 1 by Treatment Group and Visit (Female vs. Male.) Mixed Effect Model	Stage 1 Modified Intent-to-Treat Set
	14.2.3.5.6.2	Summary of the Change from Baseline in Normalized SER (D) in Stage 1 by Treatment Group and Visit (Female vs. Male)	Stage 1 Intent-to-Treat Set
14.2.3.6		Change from Baseline in Crystalline Lens Thickness at Month 36	
	14.2.3.6.1	Analysis of the Change from Baseline in Crystalline Lens Thickness (mm) in Stage 1 by Treatment Group and Visit Mixed Effect Model	Stage 1 Modified Intent-to-Treat Set
	14.2.3.6.2	Analysis of the Change from Baseline in Crystalline Lens Thickness (mm) in Stage 1 by Treatment Group and Visit Mixed Effect Model	Stage 1 Intent-to-Treat Set
14.2.3.7		Rebound Assessment	
	14.2.3.7.1.1	Rebound Assessment Based on the Change from Stage 2 Baseline (Month 36) in Normalized SER (D) at Months 42 and 48 by Stage 1 and Stage 2 Treatment Combinations and Visit	Stage 2 Modified Intent-to-Treat Set

Header	Table Number	Name	Analysis Set
	14.2.3.7.1.2	Rebound Assessment Based on the Change from Stage 2 Baseline (Month 36) in Normalized SER (D) at Months 42 and 48 by Stage 1 and Stage 2 Treatment Combinations and Visit	Stage 2 Intent-to-Treat Set
	14.2.3.7.2.1	Rebound Assessment Based on the Responders at Months 42 and 48 by Stage 1 and Stage 2 Treatment Combinations and Visit	Stage 2 Modified Intent-to-Treat Set
	14.2.3.7.2.2	Rebound Assessment Based on the Responders at Months 42 and 48 by Stage 1 and Stage 2 Treatment Combinations and Visit	Stage 2 Intent-to-Treat Set
14.2.4		Exploratory Analyses	
14.2.4.1.1		Proportion of Subjects' Eyes with Higher Myopia (SER at least 3.00 D) at Stage 1 Baseline who Show less than 0.75 D Myopia Progression (Normalized SER) at Month 36	
	14.2.4.1.1.1	Summary of the Proportion of Subjects' Eyes with Higher Myopia (SER at least 3.00 D) at Stage 1 Baseline who Show less than 0.75 D Myopia Progression (Normalized SER) at Month 36 by Treatment Group	Stage 1 Modified Intent-to-Treat Set
	14.2.4.1.1.2	Summary of the Proportion of Subjects' Eyes with Higher Myopia (SER at least 3.00 D) at Stage 1 Baseline who Show less than 0.75 D Myopia Progression (Normalized SER) at Month 36 by Treatment Group	Stage 1 Intent-to-Treat Set
14.2.4.1.2		Change from Study Baseline in Normalized SER in Stage 2	
	14.2.4.1.2.1	Analysis of the Change from Stage 2 Baseline in Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit Mixed Effect Model	Stage 2 Modified Intent-to-Treat Set
	14.2.4.1.2.4	Analysis of the Change from Stage 2 Baseline in Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit	Stage 2 Intent-to-Treat Set
	14.2.4.1.2.5	Analysis of the Change from Study Baseline in Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit Mixed Effect Model	Stage 2 Modified Intent-to-Treat Set
	14.2.4.1.2.6	Analysis of the Change from Study Baseline in Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit	Stage 2 Intent-to-Treat Set

Header	Table Number	Name	Analysis Set
14.2.4.2		Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Stage 2 Baseline in Stage 2	
	14.2.4.2.1	Summary of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Stage 2 Baseline in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit	Stage 2 Modified Intent-to-Treat Set
	14.2.4.2.2	Summary of the Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Stage 2 Baseline in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit	Stage 2 Intent-to-Treat Set
14.2.4.3		Proportion of Subjects' Eyes who Show less than 0.75 D Myopia Progression (Normalized SER) from Stage 2 Baseline in Stage 2	
	14.2.4.3.1	Summary of the Proportion of Subjects' Eyes who Show less than 0.75 D Myopia Progression (Normalized SER) from Stage 2 Baseline in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit	Stage 2 Modified Intent-to-Treat Set
	14.2.4.3.2	Summary of the Proportion of Subjects' Eyes who Show less than 0.75 D Myopia Progression (Normalized SER) from Stage 2 Baseline in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit	Stage 2 Intent-to-Treat Set
14.2.4.4		Time to Change from Stage 2 Baseline in Myopia of -0.75 D Normalized SER in Stage 2	
	14.2.4.4.1	Summary of Time to Change from Stage 2 Baseline in Myopia of -0.75 D Normalized SER in Stage 2 by Stage 1 to Stage 2 Treatment Description	Stage 2 Modified Intent-to-Treat Set
	14.2.4.4.2	Summary of Time to Change from Stage 2 Baseline in Myopia of -0.75 D Normalized SER in Stage 2 by Stage 1 to Stage 2 Treatment Description	Stage 2 Intent-to-Treat Set
14.2.4.5		New Prescriptions Given during Stage 2	
	14.2.4.5.1	Summary of the New Prescriptions Given during Stage 2	Stage 2 Modified Intent-to-Treat Set
	14.2.4.5.2	Summary of the New Prescriptions Given during Stage 2	Stage 2 Intent-to-Treat Set
14.2.4.6		Proportion of Subjects who Progressed to High Myopia (Normalized SER -6.00 D or more myopic) at Month 48 by Baseline Myopia in Stage 2	
	14.2.4.6.1	Summary of the Proportion of Subjects who Progressed to High Myopia (Normalized SER -6.00 D or more myopic) at Month 48 by Baseline Myopia in Stage 2	Stage 2 Modified Intent-to-Treat Set

Header	Table Number	Name	Analysis Set
	14.2.4.6.2	Summary of the Proportion of Subjects who Progressed to High Myopia (Normalized SER -6.00 D or more myopic) at Month 48 by Baseline Myopia in Stage 2	Stage 2 Intent-to-Treat Set
14.2.4.7		Interaction between Demographic Variables and Normalized SER in Stage 2	
	14.2.4.7.1.1	Summary of the Change from Stage 2 Baseline in Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit (6-8 years old vs. 9-10 years old)	Stage 2 Modified Intent-to-Treat Set
	14.2.4.7.1.2	Summary of the Change from Stage 2 Baseline in Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit (6-8 years old vs. 9-10 years old)	Stage 2 Intent-to-Treat Set
	14.2.4.7.2.1	Summary of the Change from Stage 2 Baseline in Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit (Baseline SER -0.50 to -3.00 D vs. -3.01 to -6.00 D D)	Stage 2 Modified Intent-to-Treat Set
	14.2.4.7.2.2	Summary of the Change from Stage 2 Baseline in Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit (Baseline SER -0.50 to -3.00 D vs. -3.01 to -6.00 D D)	Stage 2 Intent-to-Treat Set
	14.2.4.7.3.1	Summary of the Change from Stage 2 Baseline in Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit (Asian vs. Non-Asian)	Stage 2 Modified Intent-to-Treat Set
	14.2.4.7.3.2	Summary of the Change from Stage 2 Baseline in Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit (Asian vs. Non-Asian)	Stage 2 Intent-to-Treat Set
	14.2.4.7.4.1	Summary of the Change from Stage 2 Baseline in Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit (Dark Irides vs. Light Irides)	Stage 2 Modified Intent-to-Treat Set
	14.2.4.7.4.2	Summary of the Change from Stage 2 Baseline in Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit (Dark Irides vs. Light Irides)	Stage 2 Intent-to-Treat Set

Header	Table Number	Name	Analysis Set
	14.2.4.7.5.1	Summary of the Change from Stage 2 Baseline in Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit (U.S. vs. E.U.)	Stage 2 Modified Intent-to-Treat Set
	14.2.4.7.5.2	Summary of the Change from Stage 2 Baseline in Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit (U.S. vs. E.U.)	Stage 2 Intent-to-Treat Set
	14.2.4.7.6.1	Summary of the Change from Stage 2 Baseline in Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit (Female vs. Male)	Stage 2 Modified Intent-to-Treat Set
	14.2.4.7.6.2	Summary of the Change from Stage 2 Baseline in Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit (Female vs. Male)	Stage 2 Intent-to-Treat Set
14.2.4.8		Change from Stage 2 Baseline in Crystalline Lens Thickness (mm) in Stage 2	
	14.2.4.8.1	Summary of the Change from Stage 2 Baseline in Crystalline Lens Thickness (mm) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit	Stage 2 Modified Intent-to-Treat Set
	14.2.4.8.2	Summary of the Change from Stage 2 Baseline in Crystalline Lens Thickness (mm) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit	Stage 2 Intent-to-Treat Set
14.3		Safety Data Summary Tables	
14.3.1		Adverse Events	
	14.3.1.1.1	Overall Summary of Treatment-Emergent Adverse Events - Stage 1	Stage 1 Safety Set
	14.3.1.1.2	Overall Summary of Treatment-Emergent Adverse Events - Stage 2	Stage 2 Safety Set
	14.3.1.2.1.1	Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Stage 1	Stage 1 Safety Set
	14.3.1.2.1.2	Ocular Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Stage 1	Stage 1 Safety Set
	14.3.1.2.1.3	Non-Ocular Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Stage 1	Stage 1 Safety Set
	14.3.1.2.2.1	Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Stage 2	Stage 2 Safety Set
	14.3.1.2.2.2	Ocular Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Stage 2	Stage 2 Safety Set

Header	Table Number	Name	Analysis Set
	14.3.1.2.2.3	Non-Ocular Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Stage 2	Stage 2 Safety Set
	14.3.1.3.1.1	Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity – Stage 1	Stage 1 Safety Set
	14.3.1.3.1.2	Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity – Stage 1	Stage 1 Safety Set
	14.3.1.3.1.3	Non-Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity – Stage 1	Stage 1 Safety Set
	14.3.1.3.2.1	Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity – Stage 2	Stage 2 Safety Set
	14.3.1.3.2.2	Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity – Stage 2	Stage 2 Safety Set
	14.3.1.3.2.3	Non-Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity – Stage 2	Stage 2 Safety Set
	14.3.1.4.1.1	Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug – Stage 1	Stage 1 Safety Set
	14.3.1.4.1.2	Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug – Stage 1	Stage 1 Safety Set
	14.3.1.4.1.3	Non-Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug – Stage 1	Stage 1 Safety Set
	14.3.1.4.2.1	Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug – Stage 2	Stage 2 Safety Set
	14.3.1.4.2.2	Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug – Stage 2	Stage 2 Safety Set
	14.3.1.4.2.3	Non-Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug – Stage 2	Stage 2 Safety Set
	14.3.1.5.1.1	Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set
	14.3.1.5.1.2	Ocular Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set
	14.3.1.5.1.3	Non-Ocular Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set

Header	Table Number	Name	Analysis Set
	14.3.1.5.2.1	Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.5.2.2	Ocular Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.5.2.3	Non-Ocular Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.6.1.1	Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set
	14.3.1.6.1.2	Serious Ocular Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set
	14.3.1.6.1.3	Serious Non-Ocular Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set
	14.3.1.6.2.1	Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.6.2.2	Serious Ocular Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.6.2.3	Serious Non-Ocular Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.7.1.1	Serious Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set
	14.3.1.7.1.2	Serious Ocular Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set
	14.3.1.7.1.3	Serious Non-Ocular Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set
	14.3.1.7.2.1	Serious Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.7.2.2	Serious Ocular Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.7.2.3	Serious Non-Ocular Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.8.1.1	Treatment-Emergent Adverse Events Leading to Study Withdrawal by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set

Header	Table Number	Name	Analysis Set
	14.3.1.8.1.2	Ocular Treatment-Emergent Adverse Events Leading to Study Withdrawal by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set
	14.3.1.8.1.3	Non-Ocular Treatment-Emergent Adverse Events Leading to Study Withdrawal by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set
	14.3.1.8.2.1	Treatment-Emergent Adverse Events Leading to Study Withdrawal by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.8.2.2	Ocular Treatment-Emergent Adverse Events Leading to Study Withdrawal by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.8.2.3	Non-Ocular Treatment-Emergent Adverse Events Leading to Study Withdrawal by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.9.1.1	Treatment-Emergent Adverse Events Leading to Permanent Discontinuation of Study Drug by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set
	14.3.1.9.1.2	Ocular Treatment-Emergent Adverse Events Leading to Permanent Discontinuation of Study Drug by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set
	14.3.1.9.1.3	Non-Ocular Treatment-Emergent Adverse Events Leading to Permanent Discontinuation of Study Drug by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set
	14.3.1.9.2.1	Treatment-Emergent Adverse Events Leading to Permanent Discontinuation of Study Drug by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.9.2.2	Ocular Treatment-Emergent Adverse Events Leading to Permanent Discontinuation of Study Drug by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.9.2.3	Non-Ocular Treatment-Emergent Adverse Events Leading to Permanent Discontinuation of Study Drug by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.10.1.1	Treatment-Emergent Adverse Events Leading to Death by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set
	14.3.1.10.1.2	Ocular Treatment-Emergent Adverse Events Leading to Death by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set
	14.3.1.10.1.3	Non-Ocular Treatment-Emergent Adverse Events Leading to Death by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set

Header	Table Number	Name	Analysis Set
	14.3.1.10.2.1	Treatment-Emergent Adverse Events Leading to Death by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.10.2.2	Ocular Treatment-Emergent Adverse Events Leading to Death by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.10.2.3	Non-Ocular Treatment-Emergent Adverse Events Leading to Death by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.11.1.1	Treatment-Emergent Adverse Events Associated with Antimuscarinic Function by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set
	14.3.1.11.1.2	Ocular Treatment-Emergent Adverse Events Associated with Antimuscarinic Function by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set
	14.3.1.11.1.3	Non-Ocular Treatment-Emergent Adverse Events Associated with Antimuscarinic Function by System Organ Class and Preferred Term – Stage 1	Stage 1 Safety Set
	14.3.1.11.2.1	Treatment-Emergent Adverse Events Associated with Antimuscarinic Function by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.11.2.2	Ocular Treatment-Emergent Adverse Events Associated with Antimuscarinic Function by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.11.2.3	Non-Ocular Treatment-Emergent Adverse Events Associated with Antimuscarinic Function by System Organ Class and Preferred Term – Stage 2	Stage 2 Safety Set
	14.3.1.12.1.1	Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Sex – Stage 1	Stage 1 Safety Set
	14.3.1.12.1.2	Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Sex – Stage 1	Stage 1 Safety Set
	14.3.1.12.1.3	Non-Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Sex – Stage 1	Stage 1 Safety Set
	14.3.1.12.2.1	Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Sex – Stage 2	Stage 2 Safety Set
	14.3.1.12.2.2	Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Sex – Stage 2	Stage 2 Safety Set
	14.3.1.12.2.3	Non-Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Sex – Stage 2	Stage 2 Safety Set

Header	Table Number	Name	Analysis Set
	14.3.1.13.1.1	Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Race – Stage 1	Stage 1 Safety Set
	14.3.1.13.1.2	Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Race – Stage 1	Stage 1 Safety Set
	14.3.1.13.1.3	Non-Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Race – Stage 1	Stage 1 Safety Set
	14.3.1.13.2.1	Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Race – Stage 2	Stage 2 Safety Set
	14.3.1.13.2.2	Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Race – Stage 2	Stage 2 Safety Set
	14.3.1.13.2.3	Non-Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Race – Stage 2	Stage 2 Safety Set
	14.3.1.14.1.1	Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Age – Stage 1	Stage 1 Safety Set
	14.3.1.14.1.2	Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Age – Stage 1	Stage 1 Safety Set
	14.3.1.14.1.3	Non-Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Age – Stage 1	Stage 1 Safety Set
	14.3.1.14.2.1	Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Age – Stage 2	Stage 2 Safety Set
	14.3.1.14.2.2	Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Age – Stage 2	Stage 2 Safety Set
	14.3.1.14.2.3	Non-Ocular Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Age – Stage 2	Stage 2 Safety Set
14.3.2		Listings of Deaths, Other Serious, and Significant Adverse Events	
	14.3.2.1	Listing of Deaths	Safety Set
	14.3.2.2.1	Listing of Serious Ocular Treatment-Emergent Adverse Events	Safety Set
	14.3.2.2.2	Listing of Serious Non-Ocular Treatment-Emergent Adverse Events	Safety Set
	14.3.2.3.1	Listing of Treatment-Emergent Adverse Events Leading to Permanent Discontinuation of Study Drug	Safety Set
	14.3.2.3.2	Listing of Ocular Treatment-Emergent Adverse Events Leading to Permanent Discontinuation of Study Drug	Safety Set
	14.3.2.3.3	Listing of Non-Ocular Treatment-Emergent Adverse Events Leading to Permanent Discontinuation of Study Drug	Safety Set

Header	Table Number	Name	Analysis Set
	14.3.2.4.1	Listing of Treatment-Emergent Adverse Events Leading to Withdrawal from Study	Safety Set
	14.3.2.4.2	Listing of Ocular Treatment-Emergent Adverse Events Leading to Withdrawal from Study	Safety Set
	14.3.2.4.3	Listing of Non-Ocular Treatment-Emergent Adverse Events Leading to Withdrawal from Study	Safety Set
14.3.3	Not to be used for any Tables	Narratives of Deaths, Other Serious, and Certain Other Significant Adverse Events *(NOTE: this section is for Medical Writing narratives only, normally not completed by Syneos Health Biostatistics. No tables should go here.).*	
14.3.4		Abnormal Laboratory Value (each subject)	
14.3.4.1		Ophthalmic Safety Assessment Data	
	14.3.4.1.1.1	Monocular Best-Corrected Visual Acuity Results – Stage 1	Stage 1 Safety Set
	14.3.4.1.1.2	Monocular Best-Corrected Visual Acuity Results – Stage 2	Stage 2 Safety Set
	14.3.4.1.2.1	Pupil Size (mm) – Stage 1	Stage 1 Safety Set
	14.3.4.1.2.2	Pupil Size (mm) – Stage 2	Stage 2 Safety Set
	14.3.4.1.3.1	Slit Lamp Examination Results – Stage 1	Stage 1 Safety Set
	14.3.4.1.3.2	Slit Lamp Examination Results – Stage 2	Stage 2 Safety Set
	14.3.4.1.4.1	Dilated Fundus Examination Results – Stage 1	Stage 1 Safety Set
	14.3.4.1.4.2	Dilated Fundus Examination Results – Stage 2	Stage 2 Safety Set
	14.3.4.1.5.1	Tonometry - Intraocular Pressure (mmHg) – Stage 1	Stage 1 Safety Set
	14.3.4.1.5.2	Tonometry - Intraocular Pressure (mmHg) – Stage 2	Stage 2 Safety Set
14.3.4.2		Vital Signs and Physical Findings	
	14.3.4.2.1	Vital Signs and Physical Findings – Stage 1	Stage 1 Safety Set
	14.3.4.2.2	Vital Signs and Physical Findings – Stage 2	Stage 2 Safety Set
14.3.4.3		Quality of Life	
	14.3.4.3.1	Modified Amblyopia Treatment Index (mATI)	Stage 2 Safety Set

17. Index of Figures

Header	Figure Number	Name	Analysis Set
14.		Tables, Figures, and Graphs Referred to but not Included in the Text	
14.2		Efficacy Data Summary Figures and Tables	
14.2.1		Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline	
	14.2.1.1.2	Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit	Stage 1 Modified Intent-to-Treat Set
	14.2.1.2.3	Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit	Stage 1 Intent-to-Treat Set
	14.2.1.2.5	Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit	Stage 1 Modified Per Protocol Set
	14.2.1.2.7	Proportion of Subjects' Eyes who Show less than 0.5 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit	Stage 1 Per Protocol Set
14.2.2.1		Change from Baseline in Normalized SER	
	14.2.2.1.2	Normalized SER (D) in Stage 1 by Treatment Group and Visit	Stage 1 Modified Intent-to-Treat Set
	14.2.2.1.3	Change from Baseline in Normalized SER (D) in Stage 1 by Treatment Group and Visit	Stage 1 Modified Intent-to-Treat Set
	14.2.2.1.5	Normalized SER (D) in Stage 1 by Treatment Group and Visit	Stage 1 Intent-to-Treat Set
	14.2.2.1.6	Change from Baseline in Normalized SER (D) in Stage 1 by Treatment Group and Visit	Stage 1 Intent-to-Treat Set
14.2.2.2		Change from Baseline in Axial Length	
	14.2.2.2.2	Axial Length (mm) in Stage 1 by Treatment Group and Visit	Stage 1 Modified Intent-to-Treat Set
	14.2.2.2.3	Change from Baseline in Axial Length (mm) in Stage 1 by Treatment Group and Visit	Stage 1 Modified Intent-to-Treat Set
	14.2.2.2.5	Axial Length (mm) in Stage 1 by Treatment Group and Visit	Stage 1 Intent-to-Treat Set
	14.2.2.2.6	Change from Baseline in Axial Length (mm) in Stage 1 by Treatment Group and Visit	Stage 1 Intent-to-Treat Set
14.2.3.1		Proportion of Subjects' Eyes who Show less than 0.75 D Myopia Progression (Normalized SER) from Baseline	

Header	Figure Number	Name	Analysis Set
	14.2.3.1.2	Proportion of Subjects' Eyes who Show less than 0.75 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit	Stage 1 Modified Intent-to-Treat Set
	14.2.3.1.4	Proportion of Subjects' Eyes who Show less than 0.75 D Myopia Progression (Normalized SER) from Baseline in Stage 1 by Treatment Group and Visit	Stage 1 Intent-to-Treat Set
14.2.3.2		Change from Baseline in Normalized SER	
	14.2.3.2.2	Kaplan-Meier Curve for Time to Change from Baseline in Myopia Progression of -0.75 D Normalized SER in Stage 1 by Treatment Group	Stage 1 Modified Intent-to-Treat Set
	14.2.3.2.4	Kaplan-Meier Curve for Time to Change from Baseline in Myopia Progression of -0.75 D Normalized SER in Stage 1 by Treatment Group	Stage 1 Intent-to-Treat Set
14.2.4.1		Change from Baseline in Normalized SER in Stage 2	
	14.2.4.1.2.2	Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit	Stage 2 Modified Intent-to-Treat Set
	14.2.4.1.2.3	Change from Stage 2 Baseline in Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit	Stage 2 Modified Intent-to-Treat Set
	14.2.4.1.2.4.1	Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit	Stage 2 Intent-to-Treat Set
	14.2.4.1.2.4.2	Change from Stage 2 Baseline in Normalized SER (D) in Stage 2 by Stage 1 to Stage 2 Treatment Description and Visit	Stage 2 Intent-to-Treat Set

18. Index of Listings

Header	Table Number	Name	Analysis Set (Example)
16.2		Subject Data Listings	
16.2.1		Discontinued Subjects	
	16.2.1.1	Subject Disposition	Enrolled Set
16.2.2		Protocol Deviations	
	16.2.2.1	Protocol Deviations	Enrolled Set
16.2.3		Subjects Excluded from the Efficacy Analysis	
	16.2.3.1	Inclusion/Exclusion Criteria	Enrolled Set
	16.2.3.2	Exclusions from Analysis Sets	Enrolled Set
16.2.4		Demographic Data	
	16.2.4.1	Demographics	Intent-to-Treat Set
	16.2.4.2	Medical History	Intent-to-Treat Set
	16.2.4.3	Ocular History	Intent-to-Treat Set
	16.2.4.4	Baseline Disease Characteristics	Intent-to-Treat Set
	16.2.4.5	Prior and Concomitant Medications	Intent-to-Treat Set
16.2.5		Compliance	
	16.2.5.1	Study Drug Adherence	Safety Set
	16.2.5.2	Study Drug Exposure and Treatment Compliance	Safety Set
16.2.6		Individual Efficacy Response Data	
	16.2.6.1	Cycloplegic Autorefraction	Intent-to-Treat Set
	16.2.6.2	Axial Length and Crystalline Lens Thickness	Intent-to-Treat Set
		Adverse Event Listings	
	16.2.7.1	Adverse Events	Safety Set
	16.2.7.2	Severe Adverse Events	Safety Set
	16.2.7.3	Study Drug Related Adverse Events	Safety Set
	16.2.7.4	Study Drug Related Serious Adverse Events	Safety Set
16.2.8		Listing of physical examination by subject	
	16.2.8.1.1	Urine Pregnancy Test	Intent-to-Treat Set
		Other Safety Data	
	16.2.8.2.1	Best Corrected Visual Acuity	Intent-to-Treat Set
	16.2.8.2.2	Photonic Pupil Size Measurement	Intent-to-Treat Set
	16.2.8.2.3	Slit lamp Examination	Intent-to-Treat Set
	16.2.8.2.4	Dilated Fundus Examination	Intent-to-Treat Set
	16.2.8.2.5	Tonometry	Intent-to-Treat Set
	16.2.8.2.6	Modified ATI Questionnaires	Intent-to-Treat Set
	16.2.8.2.7	Telephone Contact	Intent-to-Treat Set
	16.2.8.2.8	Vital Signs and Physical Findings	Intent-to-Treat Set