A Phase 3b Open-Label Study Designed to Evaluate Tear Production Stimulated by 0.003% AR-15512

STUDY ID:

DEF512-E002

STATISTICAL ANALYSIS PLAN v.2

21 Feb 2025

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1. TITLE PAGE

A Phase 3b Open-Label Study Designed to Evaluate Tear Production Stimulated by 0.003% AR-15512

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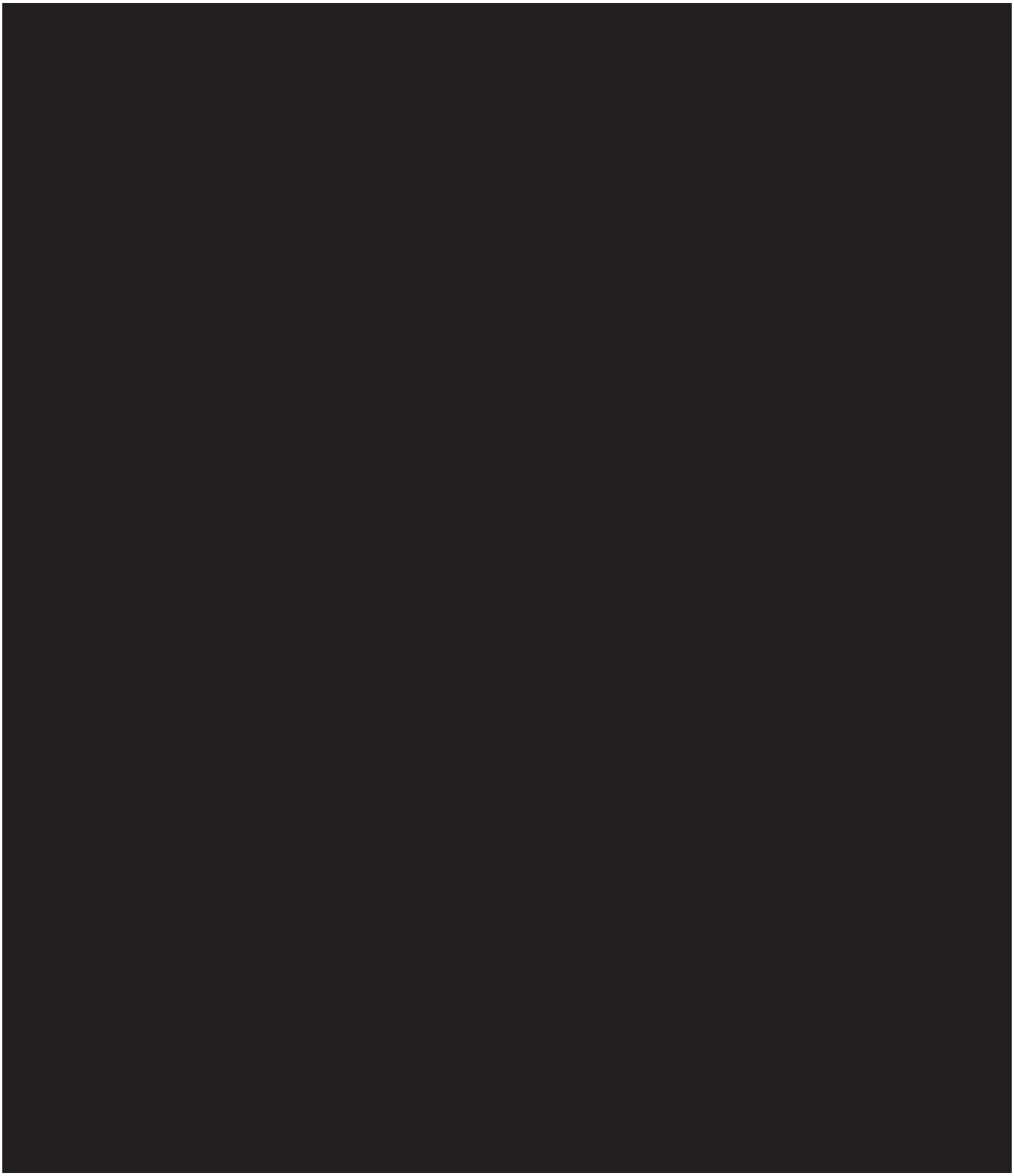

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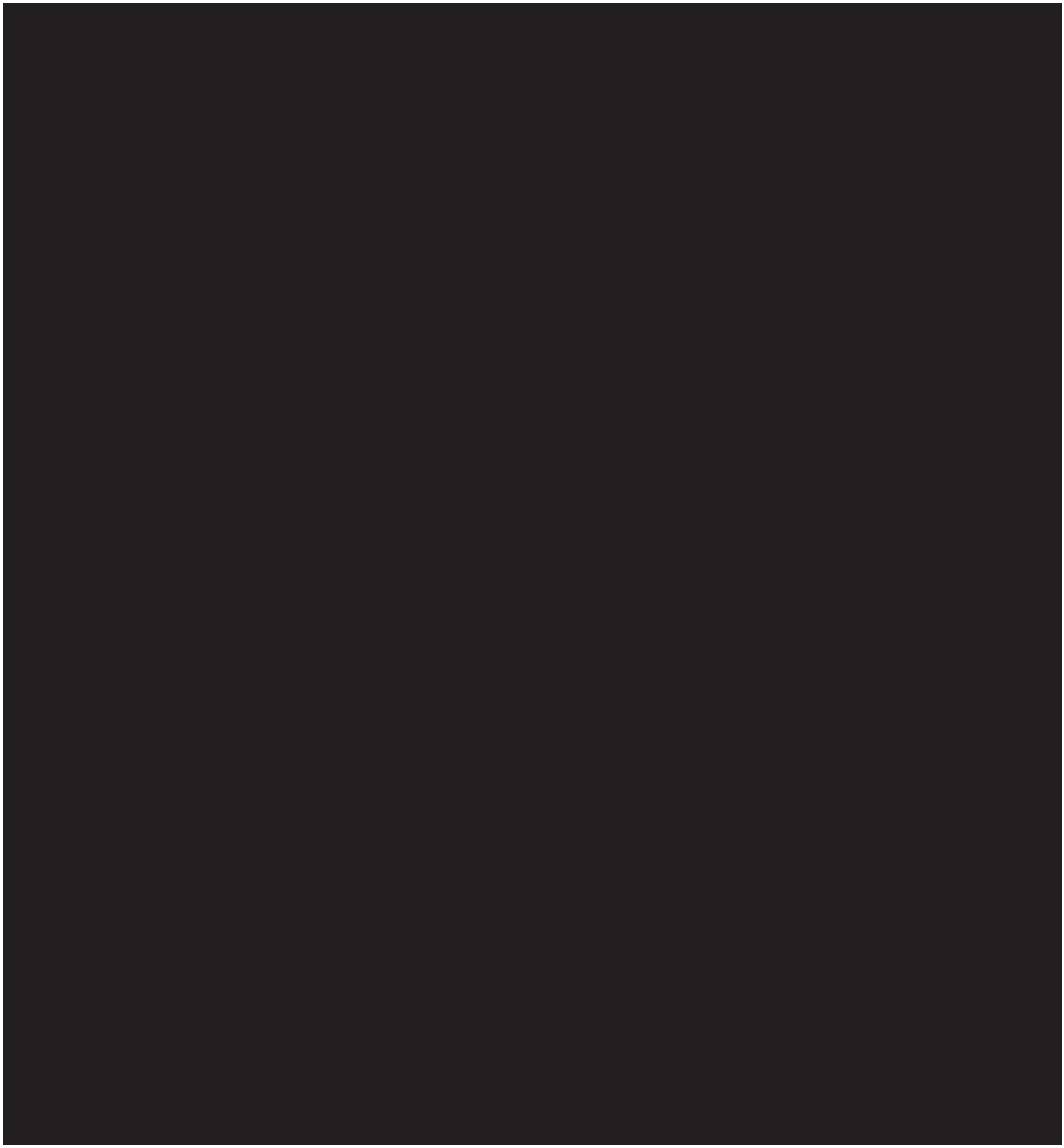

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5. DEFINITIONS AND ABBREVIATIONS

Term/Acronym	Definition
AD	Analysis Dataset
AE	Adverse Event
ATC	Anatomical Therapeutic Chemical
[redacted]	[redacted]
CI	Confidence Interval
CS	Clinically Significant
DED	Dry Eye Disease
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
ETDRS	Early Treatment of Diabetic Retinopathy Study
FAS	Full Analysis Set
H_0	Null Hypothesis
H_A	Alternative Hypothesis
ICH	International Conference on Harmonisation
[redacted]	[redacted]
logMAR	Logarithm of the Minimum Angle of Resolution
MedDRA	Medical Dictionary for Regulatory Activities
NCS	Not Clinically Significant
NEI	National Eye Institute
OCT	Optical Coherence Tomography
OD	Right Eye
OS	Left Eye
OSDI	Ocular Surface Disease Index
PDF	Portable Document Format
[redacted]	[redacted]

Term/Acronym	Definition
PT	Preferred Term
RTF	Rich Text Format
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
TEAE	Treatment-Emergent Adverse Event
TE-SAE	Treatment-Emergent Serious Adverse Event
[redacted]	[redacted]
TMH	Tear Meniscus Height
TOST	Two One-sided Tests
WHODrug	World Health Organization Drug Dictionary
WOCBP	Women of Childbearing Potential

6. INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to describe in detail the planned analyses and reporting for protocol DEF512-E002, Amendment 1, Version 2.0 dated 15JAN2025. The statistical analysis methods presented in this document will supersede the statistical analysis methods described in the clinical protocol. If additional analyses are required to supplement the planned analyses described in this SAP, they may be completed and will be identified in the clinical study report.

This SAP is being written with due consideration of the recommendations outlined in the most recent International Conference on Harmonisation (ICH) E9 Guideline[1] entitled Guidance for Industry: Statistical Principles for Clinical Trials and the most recent ICH E3 Guideline[2] entitled Guidance for Industry: Structure and Content of Clinical Study Reports.

7. STUDY OBJECTIVES

7.1 Primary Study Objective (Stage 1 and Stage 2)

The primary study objective for both Stage 1 and Stage 2 is to evaluate tear production, via tear meniscus height (TMH) as measured by optical coherence tomography (OCT), following acute administration of AR-15512 ophthalmic solution 0.003% (hereafter 0.003% AR-15512) in subjects with dry eye disease (DED).

[redacted]

8. STUDY ENDPOINTS

8.1 Primary Endpoint (Stage 1 and Stage 2)

The primary endpoint for both Stage 1 and Stage 2 is the change from baseline (pre-drop compared to 3 minutes post-drop) in TMH as measured by OCT.

[redacted]

[redacted]

8.3 Safety Endpoints (Stage 1 and Stage 2)

The safety endpoints for both Stage 1 and Stage 2 include the following:

- Corrected visual acuity
- Slit-lamp biomicroscopy
- Adverse events (AEs)

8.4 Statistical Hypotheses

Stage 1:

The primary hypothesis will focus on the change from baseline in TMH (measured at 3-minute post-drop minus pre-drop measurement) on the Full Analysis Set (FAS). The study will be considered successful if the null hypothesis (H_0) is rejected in favor of the alternative hypothesis (H_A) at the 5% (one-sided) significance level.

H_0: Mean Change from baseline in TMH = 0
H_A: Mean Change from baseline in TMH > 0

[redacted]

[redacted]

Stage 2:

Following the final analysis of Stage 1, early trends in the data were identified to support subsequent planning. Results from this final analysis have guided the transition from Stage 1 to Stage 2. [redacted] No pooling of data or analyses will occur between Stage 1 and Stage 2, ensuring the results from each stage remain distinct and separately interpretable.

The primary hypothesis for Stage 2 remains the same as for TMH in Stage 1 but analyzed independently.

[redacted]

9. STUDY DESIGN AND PROCEDURES

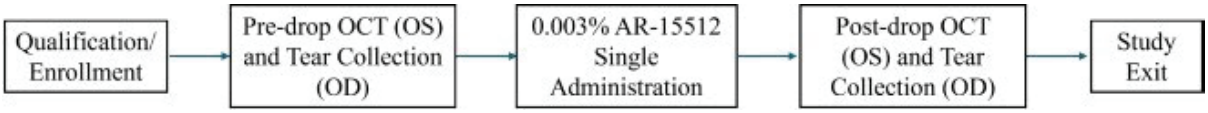
9.1 General Study Design

This is a Phase 3b, single center, open-label, single-arm, two-stage acute dosing study conducted in the United States.

Approximately 80 male and female subjects at least 18 years of age with a previous history of DED and meeting all study eligibility criteria will be enrolled. Enrollment will take place in two stages with approximately 40 subjects being enrolled in each stage. While identical in design, the two stages of

the study will be considered independent. Each of the stages will consist of one (1) visit (Screening, Enrollment, and Assessments). All subjects will be exited from the study at the end of the Study Visit. All qualified subjects post Screening will be dosed once in clinic by site staff with 0.003% AR-15512 in both eyes. The dosing will be in a staggered cadence, starting with the left eye (OS) followed by dosing of the right eye (OD) approximately 2-4 hours after completion of post-drop OCT. All subjects will undergo both baseline (pre-drop) and post-drop OCT imaging in the OS and tear collection in the OD at designated intervals. A study diagram is provided in **Figure 1**.

Figure 1. Study Design (Stage 1 and Stage 2)



Time points (pre-drop vs post-drop) will be referred to in all tables and listings as applicable to enable reviewers to understand the assessment timing without referring to the protocol visit schedule.

9.2 Schedule of Visits and Assessments

The schedule of visits and assessments is provided in **Table 1**.

Table 1. Schedule of Visits and Procedures (Stage 1 and Stage 2)

Assessment	
Informed consent	X
Demographics	X
Medical, ophthalmic, and surgical history	X
Prior or concomitant medication review	X
Urine pregnancy test (WOCBP only)	X
OSDI© Questionnaire	X
Corrected visual acuity	X
Slit lamp biomicroscopy	X
Fluorescein staining of cornea (modified NEI grading scale)	X
Inclusion and exclusion criteria review	X
Study Enrollment	X
OCT and Tear Production Assessments[1]	X
Adverse events review	X
Corrected visual acuity	X
Slit lamp biomicroscopy	X
Study Exit	X
Abbreviations: NEI = National Eye Institute; OSDI© = Ocular Surface Disease Index©; OCT = optical coherence tomography; WOCBP = women of childbearing potential [1] See details in the Manual of Procedures.	

9.3 Study Treatments

The study treatment (i.e., study intervention) in this study is 0.003% AR-15512.

Individuals who do not meet the criteria for participation in this study (screen failures) may be rescreened for eligibility up to one time if there is a reasonable possibility, in the Investigator's opinion, that the subject might meet the eligibility criteria. It is encouraged for the investigator to discuss potential rescreening with the Sponsor. The rescreened subject will be assigned a new subject ID, and the previous subject ID will be recorded in the Informed Consent electronic case report form (eCRF).

In this study, the subject ID will be in the format of xxxx-xxxx, with the first 4 characters being the site number and the last 4 characters sequentially numbered starting from 2001, which will be used to identify subjects in all datasets and listings.

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10. SAMPLE SIZE

Stage 1:

A sample size of 40 subjects provides at least 99% statistical power to detect a significant difference in mean change from baseline in TMH, at the 5% (one-sided) significance level. This calculation assumes a standard deviation (SD) of 623 µm and mean change of 550 µm [redacted]

Stage 2:

The primary objective of Stage 2 is to assess the change in TMH, assuming a 5% (one-sided significance). A sample size of 40 subjects will provide at least 99% power to detect the observed mean difference of 520 µm (SD 515 µm) for the difference between post-drop vs pre-drop measurements as identified in Stage 1. [redacted]

11. DATA PREPARATION

11.1 Input Data

Study data will primarily be recorded on the eCRFs supplied by Ora using electronic data capture (EDC) system, [redacted]

[redacted]

Final analysis will be carried out after the following have occurred:

- Database lock has occurred, including receipt of all final versions of external vendor data, with written authorization provided by appropriate Ora and Sponsor personnel.
- Protocol deviations have been identified and status defined (major/minor deviations).
- Analysis populations have been determined.

11.2 Output Data

Data from EDC and external data will be transferred to Ora Biostatistics and then mapped to analysis datasets (ADs). Raw data will be used to create subject listings along with ADs as needed, while all tables will be based on the ADs.

12. ANALYSIS POPULATIONS

12.1 Safety Analysis Set

The Safety Analysis Set will include all subjects who have received at least one dose of 0.003% AR-15512.

12.2 Full Analysis Set (FAS)

The FAS will include all subjects who have received at least one dose of 0.003% AR-15512 and have pre-drop and 3-minute post-drop TMH measurements.

[redacted]

13. GENERAL STATISTICAL CONSIDERATIONS

13.1 Unit of Analysis

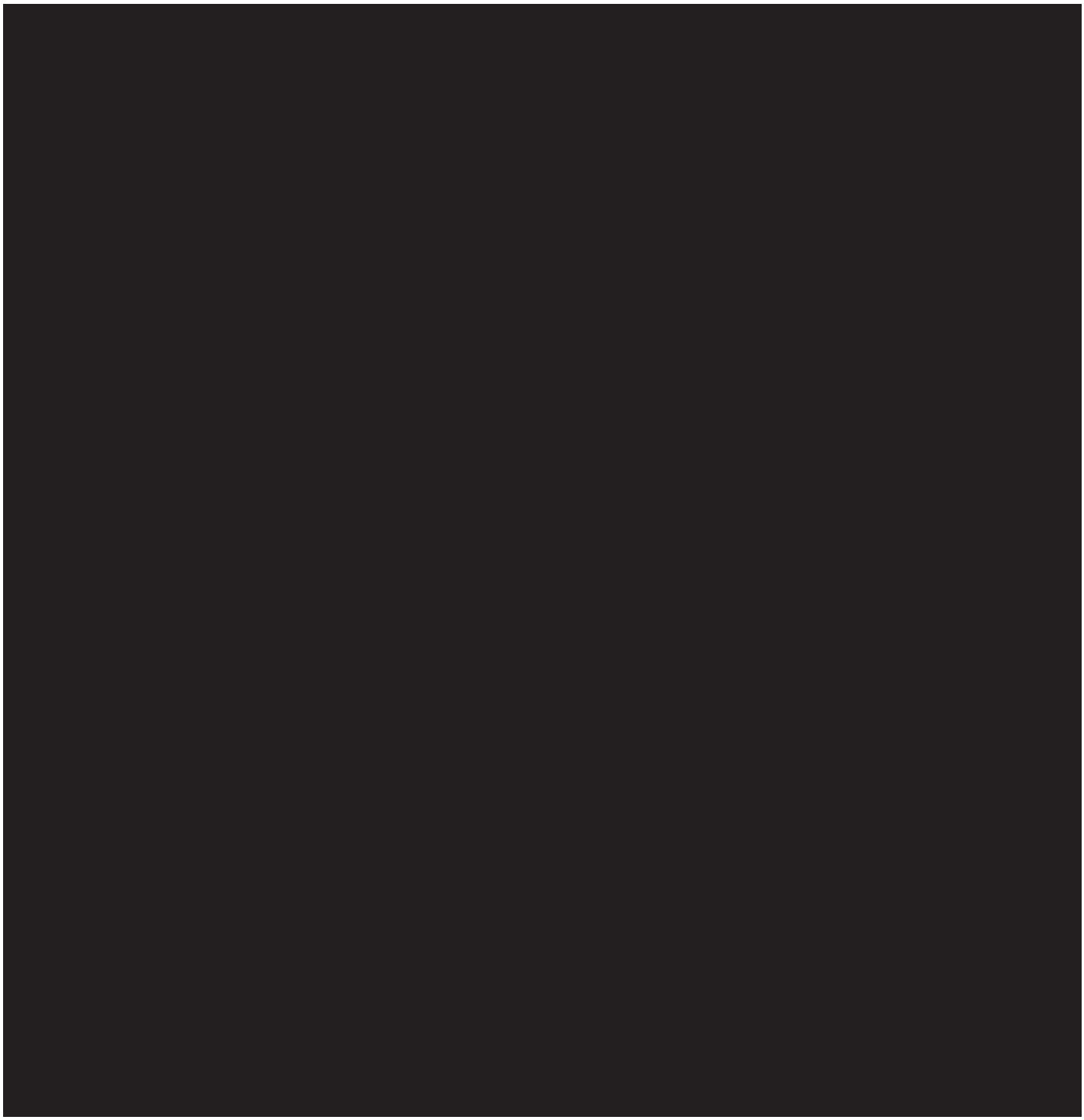
[redacted]. TEAEs will be summarized at the subject level.

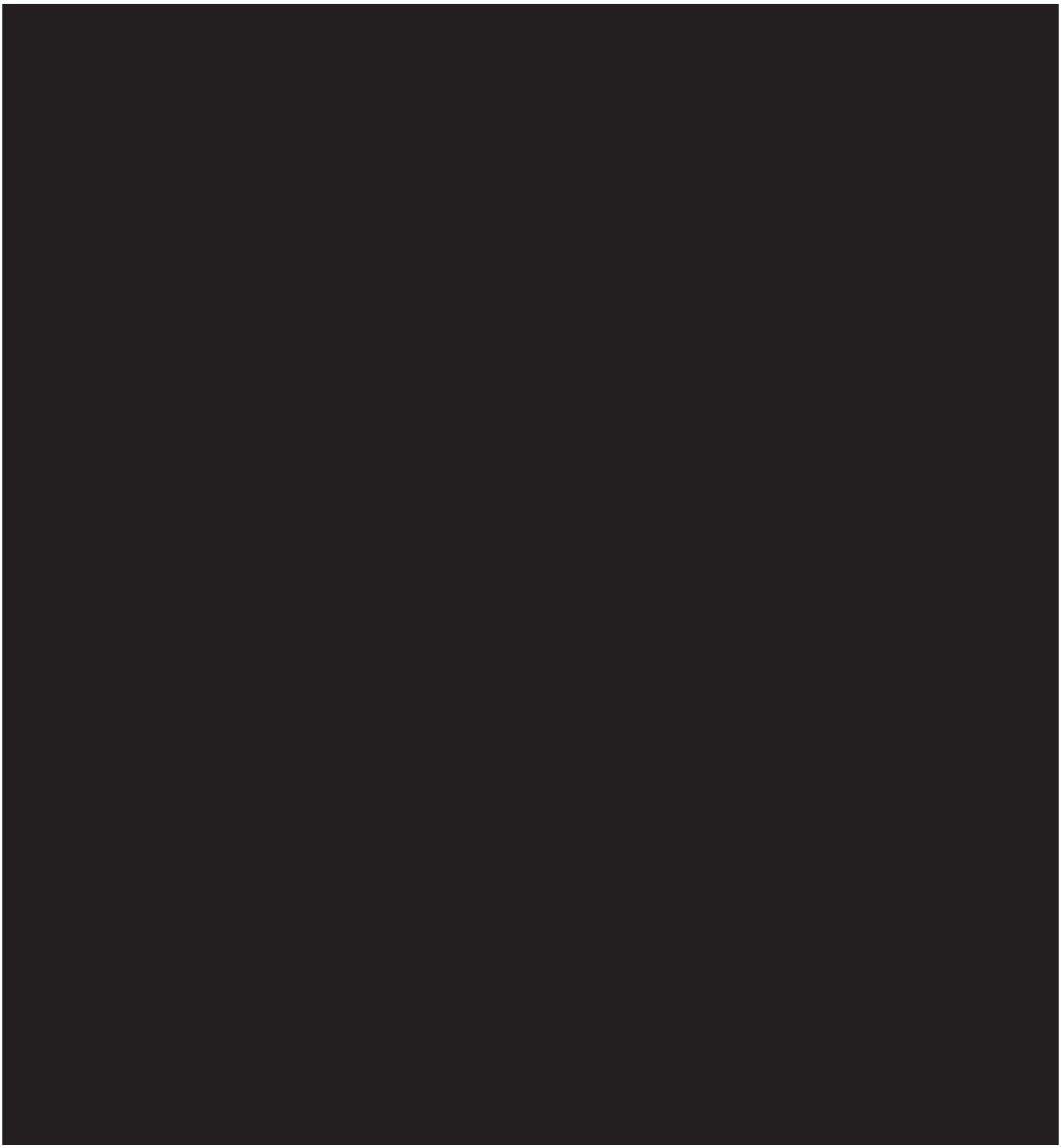
13.2 Missing or Inconclusive Data Handling

13.2.1 Missing Dates

Given this is a one visit study, all AEs will be considered as treatment-emergent unless otherwise indicated from the data that it is not treatment-emergent. No imputation of missing or partial AE dates

will be performed. All medications will be considered concomitant medications unless there are clear indications from data that the medications ended before study intervention administration. No imputation for missing or partial dates for concomitant medications will be performed.





14. DISPOSITION OF SUBJECTS

Subject disposition will be presented for Stage 1, Stage 2, and all subjects in terms of the numbers of subjects who were screened, screen failed, enrolled, and treated with 0.003% AR-15512. Numbers and percentages will be presented for subjects who were included in the FAS, [redacted] and Safety Analysis Set; and who completed the study and discontinued from the study. Subjects who are not discontinued from the study will be considered study completers. Percentages will be calculated using subjects treated with 0.003% AR-15512 as the denominator unless otherwise specified.

The reasons for premature study discontinuation will be summarized for all discontinued subjects with percentages calculated. The reasons for study discontinuation that will be summarized include AE, lost to follow up, physician decision, protocol violation, study terminated by sponsor, withdrawal by subject, and other.

The number and percentage of subjects with any deviation, major deviation, and minor deviation will be summarized for all subjects.

A subject listing will be provided for subject disposition for all subjects. In addition, subject listings will be provided for informed consent, inclusion and exclusion criteria, protocol deviations, and analysis sets.

15. DEMOGRAPHIC AND BASELINE DISEASE CHARACTERISTICS

15.1 Demographic Variables

The demographic variables collected in this study include age, biological sex, race, ethnicity, and iris color. Subjects who record more than one race will be grouped into a single category denoted as Multi-racial in the summary table and will be reported as collected in the subject listing. Iris color will be summarized for both OD and OS. Demographic variables will be summarized for Stage 1, Stage 2, and all subjects using FAS and Safety Analysis Set, separately.

Age (years) as collected will be summarized for all subjects using continuous descriptive statistics. Age will also be categorized as follows: <65 years and ≥65 years. The number and percentage of subjects will be presented for all subjects, for age category, biological sex, race, ethnicity, and iris color.

A subject listing that includes all demographic variables will be provided. In addition, a separate subject listing will be provided for the childbearing potential and pregnancy test results for female subjects.

15.2 Baseline Disease Characteristics

The pre-drop Ocular Surface Disease Index© (OSDI©) total score and total corneal fluorescein staining score for both OD and OS will be summarized using continuous descriptive statistics for Stage 1, Stage 2, and all subjects using the FAS. OSDI© questionnaire and sodium fluorescein staining of cornea (modified National Eye Institute (NEI) grading scale) are pre-treatment assessments collected during screening only. Details of the assessments are described in Section 15.2.1 and Section 15.2.2.

15.2.1 OSDI© Questionnaire

The OSDI© questionnaire consists of 12 questions regarding ocular symptom, environmental triggers, and vision-related functioning in patients with DED[3]. Each question will be rated using a 5-unit scale: 0 = None of the time, 1 = Some of the time, 2 = Half of the time, 3 = Most of the time, and 4 = All of the time. There are 7 questions (questions 6 to 12) that allow a response of "N/A" (not applicable).

OSDI© questions:

1. Eyes that are sensitive to light?
2. Eyes that feel gritty?
3. Painful or sore eyes?
4. Blurred vision?
5. Poor vision?
6. Reading?
7. Driving at night?
8. Working with a computer or bank machine (ATM)?
9. Watching TV?
10. Windy conditions?
11. Places or areas with low humidity (very dry)?
12. Areas that are air conditioned?

The total OSDI© score will be calculated in the EDC system based on the raw scores of each of the 12 questions using the following formula:

$$\text{Total OSDI© Score} = \frac{[\text{Sum of Scores for All Questions Answered}] \times 100}{[\text{Total Number of Questions Answered}] \times 4}$$

where questions answered with "N/A" will be considered unanswered and excluded from the calculation. Total OSDI© score will be recorded in EDC with one decimal place, and ranges from 0 to 100 where higher scores are worse.

A subject listing of OSDI© will be provided to present raw scores for individual questions as well as total OSDI© scores for each subject.

15.2.2 Sodium Fluorescein Staining of Cornea (Modified NEI Grading Scale)

The grading of the resulting corneal staining will be based on the modified NEI workshop grading scheme (**Figure 3**). Each of the 5 zones (zone 1: central; zone 2: superior; zone 3: temporal; zone 4: nasal; zone 5: inferior) on the cornea of each eye are to be graded (0-4 for each zone). Half (0.5) grade increments may be used. Once grading of the right cornea is complete, grading of the left cornea may take place. The total corneal staining score for each eye will be collected in eCRF, which is calculated as the sum of the grading score of 5 zones. The maximum possible score for the total

corneal staining score per eye is 20. Higher total scores indicate greater staining (or worse conditions).

A subject listing of corneal staining per eye will be provided to present the raw staining score collected for each of the 5 zones as well as the total corneal staining score for each subject.

Figure 3 Modified NEI Corneal Staining Grading Scheme

Temporal **OD** Nasal **OS** Temporal

Grade each zone using the dot count scale:

Score	Description
0	No punctate stain in the area
0.5	1–5 micropunctate stain spots
1.0	6–15 micropunctate stain spots
1.5	More than 15 micropunctate stain spots
2.0	Moderate macropunctate stain spots (involving <50% of the area)
2.5	Moderate macropunctate stain spots (involving >50% of the area)
3.0	Clumped macropunctate stain spots (involving <50% of the area)
3.5	Clumped macropunctate stain spots (involving >50% of the area)
4.0	Severe diffuse (coalescent) macropunctate stain of the area

16. MEDICAL HISTORY AND CONCOMITANT MEDICATIONS

Subject listings of medical history, prior and concomitant medications, and concomitant procedures will be generated.

16.1 Medical History

Medical history will be coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 27.1 and presented with System Organ Class (SOC) and Preferred Term (PT).

16.2 Prior and Concomitant Medications

Prior and concomitant medications will be coded using World Health Organization Drug Dictionary (WHODrug B3, September 2024) and presented with the therapeutic drug class (Anatomical Therapeutic Chemical [ATC] 4 classification) and preferred name. If the ATC 4 classification is not provided, then the next highest classification that is provided in the coding dictionary will be used. The preferred name will be defined as the active ingredient; if the active ingredient is not provided or includes more than two ingredients (e.g., multivitamins), then the drug name will be used as the preferred name.

Prior medications are defined as those medications that ended prior to the administration of the study intervention. Concomitant medications are defined as those medications listed as having been taken (1) prior to initiation of study intervention administration and continuing for any period of time following

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the administration of study intervention or (2) at any time following the administration of study intervention. Prior medications will be identified in the listing.

16.3 Concomitant Procedures

Concomitant procedures will be coded using MedDRA Version 27.1 and presented with SOC and PT.

17. DOSING COMPLIANCE AND TREATMENT EXPOSURE

All qualified subjects post screening will be dosed once in clinic by site staff with 0.003% AR-15512 in both eyes. No summaries will be performed for dosing compliance or treatment exposure. Subject listings will be provided for in-office dosing, dispensation, and accountability.

18. EFFICACY ANALYSES

Efficacy assessments are described in Section 18.1. Subject listings will be provided for each efficacy assessment. [redacted] Stage 1 efficacy analysis will be performed using the first 40 treated subjects, and Stage 2 efficacy analysis will be performed using the next 40 treated subjects independently. Results for Stage 1 and Stage 2 will be presented in separate tables.

18.1 Efficacy Assessments

18.1.1 OCT

Only the OS of subjects will be imaged with OCT, and this assessment should be performed by the Investigator, designated sub-Investigator, or trained research personnel only. The OCT imaging will occur:

a. Before 0.003% AR-15512 drop administration
b. 3 minutes ± 15 seconds after 0.003% AR-15512 drop administration

Images are recorded in the central plane of the lower eye lid, directly underneath the pupil. The primary endpoint, TMH, [redacted] measured using the OCT imaging and collected in eCRF with one decimal place. Whenever the tear meniscus is not present and the image has been confirmed to have been captured with high quality, a value of zero will be entered in EDC for TMH and TMA.

18.1.2 TEAR COLLECTION [redacted]

This assessment is performed in the OD only by the Investigator or designated sub-Investigator. Tear collection will occur:

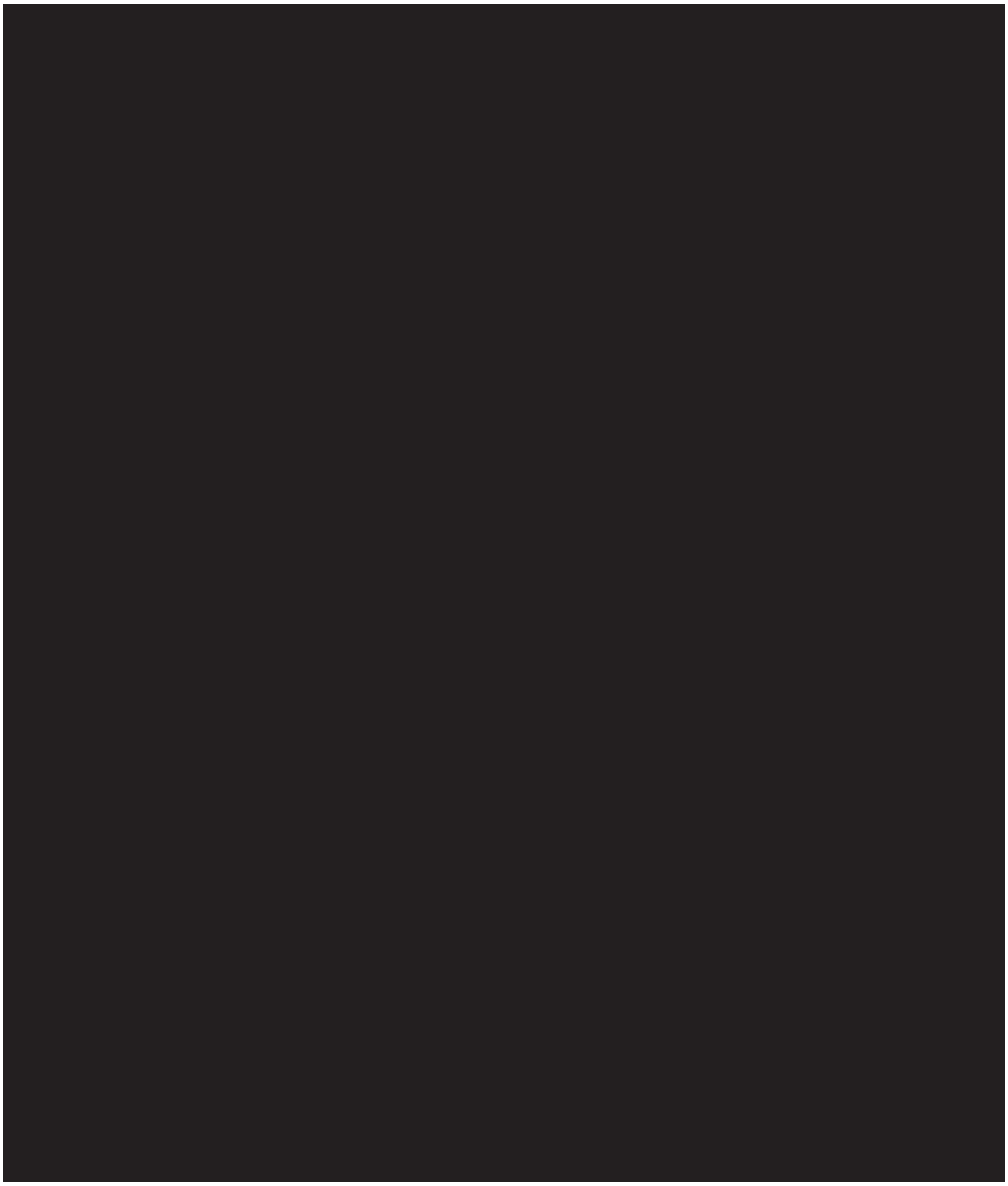
a. Before 0.003% AR-15512 drop administration
b. 3 minutes (+ 15 seconds) post 0.003% AR-15512 administration.

[redacted]

18.2 Primary Efficacy Analyses (Stage 1 and Stage 2)

The primary analysis will assess the change from baseline (pre-drop compared to 3 minutes post-drop) in TMH using OCT. A paired t-test at the 5% (one-sided) significance level using the FAS will be performed to test the pre-drop and post-drop difference in TMH. Mean difference estimate, 90% CI for the difference, and p-value will be reported. In addition, descriptive statistics of the continuous value will be reported for the observed and change from baseline results. The primary hypothesis is specified in Section 8.4. The study will be considered successful if H_0 is rejected in favor of the H_A at the 5% (one-sided) significance level. [redacted]

[redacted]



[redacted]

All safety analyses will be conducted using the Safety Analysis Set for Stage 1, Stage 2, and all subjects. No formal inferential testing will be performed.

19.1 Adverse Events

An AE is defined as any untoward medical occurrence associated with the administration of the study intervention in humans, whether or not considered to be related to the study intervention. AEs should be documented from the time the subject provides informed consent until subject participation in the study has been completed. Any medical condition present prior to informed consent which remains unchanged or improved should not be recorded as an AE. However, an AE should be recorded if the frequency, intensity, or the character of a pre-existing condition worsens during the study period beyond what would be expected from the natural progression of that condition. All AEs will be coded using the MedDRA Version 27.1.

Severity of an AE (mild, moderate, and severe) is defined as a qualitative assessment of the degree of intensity of an AE as determined by the investigator or reported to them by the subject. The relationship of each AE (not related, unlikely related, possibly related, and related) to the study intervention or procedure, and the expectedness of each AE (unexpected and expected) should be determined by the Investigator.

Treatment-emergent adverse events (TEAEs) are defined as any event that occurs or worsens on or after the dose of study intervention. Only TEAEs will be summarized, however all AEs (for all subjects) collected in the eCRF will be presented in data listings.

An overall summary will be presented that includes the number of events and the number and percentage of subjects who experienced at least one TEAE. This summary will also include breakdowns of TEAEs further categorized as ocular (OD, OS, and OU separately) or non-ocular, TEAEs related (defined as either related or possibly related) to study intervention, treatment-emergent serious adverse events (TE-SAEs), TE-SAEs related to study intervention, TEAEs leading to study intervention discontinuation, TEAEs leading to death, TEAEs by maximum severity, and TEAEs by strongest relationship to study intervention.

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Additional summaries of TEAEs will be provided showing the number and percentage of subjects who experienced at least one TEAE and classified by MedDRA SOC and PT. If a subject reports multiple TEAEs to the same SOC or multiple PTs within the same SOC, the subject will be counted only once within that SOC or PT. In the summaries, SOCs will be listed in ascending alphabetical order; PTs will be listed in order of descending frequency for all subjects within each SOC.

Separate summaries by SOC and PT will be provided for the following categories of AEs:

- TEAEs
- Treatment-related TEAEs

All AEs will be presented in a subject listing.

19.2 Corrected Visual Acuity

The logarithm of the minimum angle of resolution (logMAR) visual acuity will be assessed in both eyes pre-drop during screening and post-drop after study intervention administration using an Early Treatment Diabetic Retinography Study (ETDRS) Series 2000 chart.

The observed and change from baseline in logMAR will be summarized for each eye (OD and OS) using continuous descriptive statistics. A subject listing of corrected visual acuity will be produced. EDC will have change from pre-drop logMAR collected, which will be presented in the listing. The table summary of change from baseline will be based on calculated values.

19.3 Slit-Lamp Biomicroscopy

A slit-lamp biomicroscopy examination of the eyelid (erythema, edema), conjunctiva (hyperemia, edema), cornea (edema, staining/erosion), anterior chamber (cells, flare), iris, and lens (lens status, lens opacity for phakic only) will be performed pre-drop during screening and post-drop after study intervention administration. The findings will be graded for clinical significance (CS) and non-clinical significance (NCS).

Shift tables of score values will be provided comparing post-drop measurements to baseline (i.e. pre-drop measurement) for OD and OS separately. A subject listing of the slit-lamp biomicroscopy parameters will be produced.

20. INTERIM ANALYSES

An interim analysis in Stage 1 for futility (i.e., final analysis for Stage 1) will be performed on OCT TMH [redacted] data after approximately 40 subjects have completed and exited from the study. During the interim analysis period, database eCRF forms for the enrolled subjects will be locked to prevent the site from updating any data after interim analysis and study enrollment will be temporarily paused. The primary purpose of the interim analysis is to identify early trends in the data for administrative planning purposes. Results from the planned futility analysis will guide the decision to either continue or terminate the study. Stage 1 data will also serve as pilot data for Stage 2, helping to inform Stage 2 design.

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The interim analysis summaries for Stage 1 are identified in Section 23.1 in italicized font. The decision to either continue or terminate the study will be made based on the analysis results for TMH primarily; [redacted] There will be no interim analysis in Stage 2.

21. CHANGES FROM PROTOCOL-STATED ANALYSES

There are no changes from protocol-stated analyses.

22. REFERENCES

1. *ICH Harmonised Tripartite Guideline: Statistical Principles for Clinical Trials E9*. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. 05 February 1998.

2. *ICH Harmonised Tripartite Guideline: Structure and Content of Clinical Study Reports E3*. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. 30 November 1995.

3. Schiffman, R. M., M. D. Christianson, G. Jacobsen, J. D. Hirsch and B. L. Reis (2000). "Reliability and validity of the Ocular Surface Disease Index." Arch Ophthalmol 118(5):615-621.

4. Schuirmann, D. J. (1987). "A comparison of the two one-sided tests procedure and the power approach for assessing the equivalence of average bioavailability." J Pharmacokinet Biopharm 15(6): 657-680.

23. PLANNED OUTPUT

23.1 Tables

Tables that will be included in the Stage 1 interim analysis are shown in italicized font. No topline is planned for this study.

Number	Title	Population
Table 14.1.1	Subject Disposition	All Subjects
Table 14.1.2.1.1	Demographics	Full Analysis Set
Table 14.1.2.1.2	Demographics	Safety Analysis Set
Table 14.1.2.2	Baseline Disease Characteristics	Full Analysis Set
Table 14.2.1.1	*Actual and Change from Baseline in Tear Meniscus Height (µm) Assessed by OCT*	*Full Analysis Set*
Table 14.2.1.1.s2	Stage 2: Actual and Change from Baseline in Tear Meniscus Height (µm) Assessed by OCT	Full Analysis Set

Number	Title	Population
Table 14.2.1.2	Actual and Change from Baseline in Tear Meniscus Height (µm) Assessed by OCT	Per Protocol Set
Table 14.2.1.2.s2	Stage 2: Actual and Change from Baseline in Tear Meniscus Height (µm) Assessed by OCT	Per Protocol Set
[redacted]		
Table 14.3.1.1	Overall Summary of Treatment-Emergent Adverse Events	Safety Analysis Set
Table 14.3.1.2	Treatment-Emergent Adverse Events by System Organ Class and Preferred Term	Safety Analysis Set
Table 14.3.1.3	Treatment-Related TEAEs by System Organ Class and Preferred Term	Safety Analysis Set
Table 14.3.2	Actual and Change from Baseline in Corrected Visual Acuity in logMAR Score	Safety Analysis Set
Table 14.3.3	Shift from Baseline in Post-drop Slit-Lamp Biomicroscopy Results	Safety Analysis Set

23.2 Listings

Number	Title	Population
Listing 16.2.1.1	Subject Disposition	All Subjects
Listing 16.2.1.2	Informed Consent	All Subjects
Listing 16.2.2.1	Inclusion/Exclusion Criteria	All Subjects
Listing 16.2.2.2	Protocol Deviations	Enrolled Subjects

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Number	Title	Population
Listing 16.2.3	Analysis Sets	Enrolled Subjects
Listing 16.2.4.1.1	Demographics	Enrolled Subjects
Listing 16.2.4.1.2	Childbearing Potential and Pregnancy Tests	Enrolled Female Subjects
Listing 16.2.4.2	Medical History	Enrolled Subjects
Listing 16.2.4.3	Prior and Concomitant Medications	Enrolled Subjects
Listing 16.2.4.4	Concomitant Procedures	Enrolled Subjects
Listing 16.2.4.5	Ocular Surface Disease Index (OSDI) Questionnaire	Enrolled Subjects
Listing 16.2.4.6	Fluorescein Staining of Cornea – Modified NEI Grading Scale	Enrolled Subjects
Listing 16.2.5.1	In-Office Dosing prior to OCT in Left Eye and prior to Tear Collection in Right Eye	Enrolled Subjects
Listing 16.2.5.2	Study Drug Dispensation	Enrolled Subjects
Listing 16.2.5.3	Accountability	Enrolled Subjects
Listing 16.2.6.1	Tear Meniscus Height (TMH; µm) [redacted] by Optical Coherence Tomography (OCT) in Left Eye	Enrolled Subjects
Listing 16.2.6.2.1	Tear Collection in Right Eye	Enrolled Subjects
[redacted]		Enrolled Subjects
Listing 16.2.7	Adverse Events	All Subjects
Listing 16.2.8.1	Corrected Visual Acuity (CVA)	Enrolled Subjects
Listing 16.2.8.2	Slit-Lamp Biomicroscopy	Enrolled Subjects

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