1. TITLE PAGE

A Randomized, Double-masked, Vehicle-controlled Study Evaluating the Efficacy and Safety of OCS-01 ophthalmic suspension in the Treatment of Inflammation and Pain Following Cataract Surgery

Sponsor:	**Oculis Operations Sàrl** **Avenue de la Gare 39** **1003 Lausanne, Switzerland**
Protocol Number:	**DX-220**
Ora Study Number:	[redacted]
Protocol Title:	**A Randomized, Double-masked, Vehicle-controlled Study Evaluating the Efficacy and Safety of OCS-01 ophthalmic suspension in the Treatment of Inflammation and Pain Following Cataract Surgery**
ASAP Version Number:	**Version 1.0**
ASAP Version Date:	**11-DEC-2024**
Prepared by:	**Ora, Inc. (Ora)** **138 Haverhill St, Suite 100** **Andover, MA 01810** **Tel: (978) 685-8900** **Fax: (978) 689-0020**

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3. APPROVALS

This Abbreviated Statistical Analysis Plan was subjected to critical review and has been approved by the following personnel:

APPROVALS

If eSignature is used:
- *Attach eSig platform's audit log page and/or include a stamp that specifies the tool/platform used.*
- *Use either a Date Field option or a Text Field to ensure the date is entered in dd-MMM-yyyy format.*

Sponsor Representative by Signature: *(indicating this document has been reviewed and approved)*

Name	Title	Signature or eSignature	Date (dd-MMM-yyyy)
[redacted]	[redacted]	[redacted]	Dec 12, 2024
[redacted]	[redacted] Oculis Operations Sàrl	[redacted]	Dec 12, 2024

Ora Representative by Signature: *(indicating this document has been reviewed and approved)*

Name	Title	Signature or eSignature	Date (dd-MMM-yyyy)
[redacted]	[redacted]	[redacted]	Dec 11, 2024
[redacted]	[redacted]	[redacted]	Dec 12, 2024

Ora QC Review: *(indicating this document has been reviewed and approved)*

Name	Title	Signature or eSignature	Date (dd-MMM-yyyy)
[redacted]	[redacted]	[redacted]	Dec 12, 2024

DOCUMENT VERSION HISTORY

Document Version Number	Summary of Changes	Author Name	Document Version Date
1.0	Initial Release	[redacted]	11-DEC-2024

4. DEFINITIONS AND ABBREVIATIONS

Term/Acronym	Definition
ASAP	Abbreviated Statistical Analysis Plan
ADaM	Analysis Data Model
AE	Adverse Event
ATC	Anatomical Therapeutic Chemical
CS	Clinically Significant
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
ETDRS	Early Treatment of Diabetic Retinopathy Study
FAS	Full Analysis Set
ICH	International Conference on Harmonisation
IOP	Intraocular Pressure
logMAR	Logarithm of the Minimum Angle of Resolution
MedDRA	Medical Dictionary for Regulatory Activities
NCS	Not Clinically Significant
PDF	Portable Document Format
PP	Per Protocol
PT	Preferred Term
QD	*Quaque die* (Once Daily)
RTF	Rich Text Format
SAE	Serious Adverse Event
SD	Standard Deviation
SDTM	Study Data Tabulation Model
SOC	System Organ Class
TEAE	Treatment-Emergent Adverse Event

Term/Acronym	Definition
TE-SAE	Treatment-Emergent Serious Adverse Event
VA	Visual Activity
WHODrug	World Health Organization Drug Dictionary

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5. INTRODUCTION

The purpose of this Abbreviated Statistical Analysis Plan (ASAP) is to describe in detail the planned analyses to satisfy the clinical study report (CSR) synopsis for protocol DX-220, Version 1.0 dated 25SEP2023**.** 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 ASAP, they may be completed and will be identified in the CSR.

This ASAP is being written with due consideration of the recommendations outlined in the most recent International Conference on Harmonisation (ICH) E9 Guideline entitled Guidance for Industry: Statistical Principles for Clinical Trials, the Food and Drug Administration (FDA) Guidance for Industry: Submission of Abbreviated Reports and Synopses in Support of Marketing Applications, and the most recent ICH E3 Guideline entitled Guidance for Industry: Structure and Content of Clinical Study Reports.



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6. STUDY OBJECTIVES

The primary objective of this study is to evaluate the efficacy and safety of OCS-01 once daily (QD) compared to vehicle in the treatment of inflammation and pain following cataract surgery.

6.1 Primary Study Objectives

The primary study objectives are the following:

- To evaluate the efficacy of OCS-01 to control inflammation and pain in subjects after cataract surgery.

[redacted]

7. STUDY ENDPOINTS

Efficacy measures from the protocol are listed below but will not be analyzed.

7.1 Primary Efficacy Measures

The primary endpoints include the following, listed in hierarchical order:

- Absence of anterior chamber cells (i.e., score of "0") at Visit 6 [redacted]
- Absence of pain (i.e., score of "0") at Visit 4 [redacted]

[redacted]

7.3 Safety Measures

The safety endpoints include the following:

- Adverse event (AE) rates
- Change from baseline in pin-hole visual acuity (VA) (without any other correction) as measured on the Early Treatment of Diabetic Retinopathy Study (ETDRS) chart
- Change from baseline of intraocular pressure (IOP)
- Slit lamp biomicroscopy parameters
- Dilated indirect ophthalmoscopy parameters

[redacted]

8. STUDY DESIGN AND PROCEDURES

8.1 General Study Design

This is a multi-center, randomized, double masked, vehicle-controlled study, designed to evaluate the efficacy and safety of OCS-01 compared to vehicle in treating inflammation and pain following cataract surgery.

Subjects will be randomized 1:1 to receive OCS-01 or vehicle QD. Subjects will dose 1 drop in the study eye QD for 14 days, beginning 1-day post-surgery in the operated eye (administration of first dose will be performed in the clinic on [redacted] including screening at Visit 1 [redacted] [prior to surgery]).

Study visits will be referred to in all tables and listings as the scheduled visit name and planned study day corresponding to the visit to enable reviewers to understand the assessment timing without referring to the protocol visit schedule.

8.2 Schedule of Visits and Assessments

The schedule of visits and assessments is provided in Appendix A.

8.3 Study Treatments

Study eyes will be treated with either OCS-01 (Dexamethasone Ophthalmic Suspension, 1.5% [15 mg/mL]) (QD) or vehicle ophthalmic suspension (QD) during the treatment period of the study.

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10. DATA PREPARATION

10.1 Input Data

Study data will primarily be recorded on the electronic Case Report Forms (eCRFs) supplied by Ora using electronic data capture (EDC) system iMedNet.

When all prerequisites for database lock have been met the database will be locked. Following database lock, approval will be obtained from the Sponsor to unmask the study. Any changes to the database after data have been locked can only be made with the approval of the Sponsor in consultation with Ora.

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

- Database lock has occurred 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.
- Randomized and actual treatment codes have been unmasked.

10.2 Output Data

Data from EDC will be transferred to Ora Biostatistics and incorporated into standard formats following the Study Data Tabulation Model (SDTM). Data will then be mapped to analysis datasets using the Analysis Data Model (ADaM). Both SDTM- and ADaM-formatted data will be used to create the subject listings, while all tables and figures will be based on the ADaM-formatted data. The SDTM and ADaM versions, implementation guide versions, and Pinnacle 21 version will be documented in the respective reviewer's guides in the final CDISC package.

11. ANALYSIS POPULATIONS

11.1 Full Analysis Set

The FAS will consist of all randomized subjects, analyzing subjects under the treatment to which they were randomized.

11.2 Per Protocol Set

The Per Protocol (PP) set, as defined in the protocol, will not be created because its main purpose is to test the robustness of the primary efficacy analyses, which are not being performed. However, major protocol deviations related to study inclusion or exclusion criteria, conduct of the trial, subject management, or subject assessments will be identified prior to unmasking treatment.

11.3 Safety Set

The Safety Set includes all randomized subjects who receive at least 1 dose of study medication. The Safety Set will be analyzed as treated and will be used for the safety analyses. No data will be excluded for any reason.

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12. GENERAL STATISTICAL CONSIDERATIONS

12.1 Unit of Analysis

The unit of analysis in this study will be the study eye for all ocular safety summaries and the subject for all non-ocular summaries.

The non-study eye will be referred to as the fellow eye. Fellow eye safety summaries will also be presented as appropriate.

12.2 Missing or Inconclusive Data Handling

12.2.1 Missing Safety Assessments

In general, there will be no imputation of missing data other than for partial or missing dates where complete dates are required to flag data as treatment-emergent or concomitant with treatment. Partial/missing start and end dates for AEs and concomitant medications will be imputed as follows:

Partial/missing start date:

- Start dates with missing day only will be imputed as the 1st of the month unless the month and year are same as the month and year of first dose of study medication, in which case missing day will be imputed as the first dose day of study medication.
- Start dates with both day and month missing will be imputed as 01 Jan unless the year is same as the year of first dose of study medication, in which case missing day and month will be imputed as the first dose day and month of study medication.
- Completely missing start dates will be imputed as the first dose date of study medication unless the end date is on or before the first dose date of study medication, in which case missing date will be imputed as 01 Jan of the same year as the end date.

Partial/missing end date:

- End dates with missing day only will be imputed as the last day of the month unless the month and year are the same as the month and year of the last dose of study medication, in which case missing day will be imputed as the last dose day of study medication.
- End dates with both day and month missing will be imputed as 31 Dec unless the year is same as the year of the last dose of study medication, in which case missing day and month will be imputed as the last dose day and month of study medication.
- If the end date is completely missing and the ongoing flag is checked, then the date will not be imputed unless the death date is available, in which case the missing date will be imputed as the death date. If ongoing is not checked while the end date is missing, then the missing end date will be imputed as the last dose date of study medication. For concomitant medications, if the end date is missing and the ongoing flag is checked, then the medication is considered concomitant to the treatment.

The original dates will be displayed in data listings, and the imputed dates will be used in derivations only (study day, treatment-emergence status, etc). The formats “YYYY-MM-DD” and “hh:mm” will be

used to report dates and times, respectively, in the listings and tables. Additionally, the missing or unknown (UK/UNKN) month and day will be replaced by “UK” and year will be replaced by “UNKN”.

12.3 Definition of Baseline

Baseline is defined as the last measurement prior to first dose of study medication.

12.4 Data Analysis Conventions

All data analyses described in this ASAP will be performed by Ora. Statistical programming and analyses will be performed using SAS® Version 9.4 or higher. Output will be provided in rich text format (RTF) for tables and portable document format (PDF) for tables, listings, and figures using landscape orientation.

Summaries for continuous and ordinal variables will include the number of observations (n), arithmetic mean, standard deviation (SD), median, minimum, and maximum. Minima and maxima will be reported with the same precision as the raw values; means and medians will be presented to one additional decimal place than reported in the raw values. Standard deviations will be presented to two additional decimal places than reported in the raw values. Summaries for discrete variables will include counts and percentages. All percentages will be rounded to one decimal place (i.e., XX.X%). Differences between active treatment and vehicle will be calculated as, Active – Vehicle, and change from baseline will be calculated as, Follow-up Visit – Baseline.

Unless otherwise specified, summaries will be presented by treatment group and, where appropriate, visit. Listings will be presented by subject number, treatment group, visit, time point, and parameter as applicable based on all randomized subjects unless otherwise specified.

12.5 Adjustments for Multiplicity

No adjustments for multiplicity will be made since no formal hypothesis testing will be performed.

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13. DISPOSITION OF SUBJECTS

Subject disposition will be presented in terms of the numbers of subjects who were screened, screen failures, and randomized, by treatment group and overall, for all screened subjects. The numbers of subjects who were included in the Safety Set as well as the numbers and percentages of subjects who completed the study and discontinued from the study will be presented by treatment group and overall for all treated subjects. Subjects who are not discontinued from the study will be considered study completers. The reasons for discontinuation will be summarized by treatment group and overall for all discontinued subjects, and percentages will be calculated using discontinued subjects as the denominator. The reasons for study discontinuation that will be summarized include: adverse event, administrative reasons, protocol violation, study terminated by sponsor, withdrawal by subject, principal investigator's decision, lack of efficacy, and other. The number and percentage of subjects with any deviation, major deviation, and minor deviation will be summarized by treatment group and overall, for all treated subjects.

The reasons for screen failure (i.e., subject did not meet eligibility criteria) will be displayed with the percentages calculated using total number of screen failures as the denominator.

Details of the study randomization, including study site, randomization date, randomized treatment, and actual treatment, will be provided within a subject listing.

A subject listing for subject disposition will include study completion or discontinuation date, study completion status, and the primary reason for study discontinuation (if applicable).

For protocol deviations, a subject listing will be provided that includes the date of the deviation, visit at which the deviation occurred, the deviation category, the deviation description, if the deviation was related to COVID-19, and the classification of whether the deviation was judged to be major or minor in a masked review prior to database lock.

A subject listing of inclusion/exclusion criteria will include whether all eligibility criteria were met, the specific eligibility criterion which was not met (if applicable), and the visit at which the eligibility criterion was not met (if applicable).

A subject listing of analysis population inclusion will include whether criteria were met for inclusion in the FAS and Safety Set.

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14. DEMOGRAPHIC AND BASELINE DISEASE CHARACTERISTICS

14.1 Demographic Variables

The demographic variables collected in this study include age, gender, ethnicity, race, and iris color. Subjects who record more than one race will be grouped into a single category denoted as multi-racial. Iris color will be summarized at the eye level. Demographic variables will be summarized for the Safety Set.

Age (years) will be summarized, overall and by actual treatment group, 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, overall and by actual treatment, for age category, gender, ethnicity, race, iris color, and study site.

A subject listing that includes all demographic variables will be provided.

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15. MEDICAL HISTORY AND CONCOMITANT MEDICATIONS

Separate listings of medical history and concomitant medications for ocular and non-ocular data, as well as a listings for IOP-lowering medications, IOP-lowering procedures, concomitant procedures, and cataract surgery data will be generated.

15.1 Medical History

Medical history will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Non-ocular medical history will be summarized using discrete summary statistics and presented by actual treatment group and overall for all subjects at the subject level by System Organ Class (SOC) and Preferred Term (PT) using the Safety Set. Ocular medical history will be similarly summarized at the subject level. If a subject reports the same PT multiple times within the same SOC, that PT will only be reported once within that SOC. As with the PT, if a subject reports multiple conditions within the same SOC, that SOC will only be reported once. In the summaries, SOCs are ordered in ascending alphabetical order, and PTs within an SOC are sorted by descending frequency for all subjects.

15.2 Concomitant Medications

Concomitant medications will be coded using the World Health Organization Drug Dictionary (WHODrug) Global, B3, 01Sep2023 and summarized to 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 summarized as the preferred name.

Prior medications are defined as those medications with an end date before the date of first dose of study drug medication. Concomitant medications are defined as those medications listed as having been taken (1) prior to first dose of study medication and continuing for any period of time following the first dose of study medication or (2) at any time following the first dose of study medication.

Concomitant medications will be summarized using the Safety Set. Medications will be tabulated for each actual treatment group using frequencies and percentages. Subjects may have more than one medication per ATC text. At each level of subject summarization, a subject will be counted once if they report one or more medications. Percentages will be based on the number of subjects in each actual treatment group. In the summaries, ATC Classes and preferred names will be presented in ascending alphabetical order.

All medications utilized for lowering IOP or for rescue will be noted in the subject listing of prior and concomitant medications. IOP-lowering medications and rescue medications are each a subset of medications where the investigator has indicated on the eCRF that the medication was used to lower IOP or rescue.

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The number and percentage of subjects initiating IOP-lowering medications will be presented by actual treatment group for each post-baseline visit as well as across all post-baseline visits for the Safety Set.

15.3 Concomitant Procedures

Concomitant procedures will be coded using MedDRA Version 26.1. Concomitant procedures will be listed but not summarized.

16. DOSING COMPLIANCE AND TREATMENT EXPOSURE

Details of individual administrations of study medication done at home by subjects are not captured within the clinical database, therefore dosing compliance will not be summarized.

The number and percent of subjects receiving at least one dose of study medication (i.e., Safety Set) will be summarized as part of subject disposition.

Although not captured directly on the eCRF, additional variables related to study drug administration will also be derived for summarization:

- Study drug interruption (yes/no), where interruptions will be identified via presence of a TEAE where action taken with study drug was marked as “drug interrupted” or a protocol deviation indicating study drug was interrupted.

- Premature discontinuation of study drug (yes/no), where discontinuations will be identified via presence of a TEAE where action taken with study drug was marked as “drug withdrawn” or a protocol deviation indicating study drug was prematurely discontinued. Subjects who discontinue the study prior to Visit 6 ([redacted] will also be reviewed to verify if study drug was prematurely discontinued or not.

- Study drug completion, defined as those subjects where premature discontinuation of study drug is not equal to “yes”.

A masked data review will be conducted prior to database lock and unmasking to identify any other cases of study drug interruption or premature discontinuation of study drug which are known to have occurred, but are not identified through the criteria above. The classifications from this final review will be used for analysis.

The number and percentage of subjects with study drug interruption, premature discontinuation of study drug, and study drug completion will be presented by actual treatment group.

Subject data listings will be generated to present details of study drug assignment, study drug replacement, as well as first instillation of study medication performed in-clinic on Visit 2 ([redacted]
Details about study drug accountability will also be listed.

17. EFFICACY ANALYSES

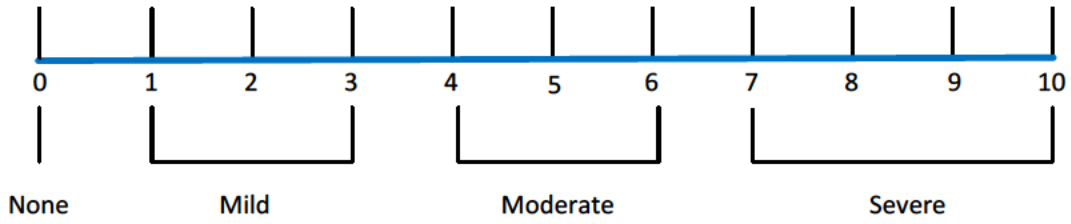
The primary efficacy variables are the following:

- Absence of anterior chamber cells, defined as a score of "0," at Visit 6 ([redacted]
- Absence of pain, defined as a score of "0," at Visit 4 ([redacted]

The anterior chamber cell score for study eyes will be recorded as well as the anterior chamber cell count if the actual number of cells observed is 10 cells or fewer (only white blood cells should be counted; red blood cells and pigment cells should not be counted). The assessment of anterior chamber cells will be performed prior to any other procedure that requires dilation of the pupil, such as dilated indirect ophthalmoscopy, to avoid cells from being introduced into the anterior chamber. The 5-unit grading scale for anterior chamber cells is from 0 to 4 where 0 = 0 cells, 1 = 1 to 10 cells, 2 = 11 to 25 cells, 3 = 26 to 50 cells, and 4 = >50 cells. Anterior chamber cell status will be classified as "Absent" for a grade of 0 or "Present" for a grade of 1 to 4.

Ocular pain in study eyes will be assessed by the subject utilizing a pain rating scale graded from 0 to 10. Subjects will assess the level of pain they are experiencing in the study eye at the time of the assessment. The examiner will ask the subject the following question, in reference to the below figure, and will record the number selected by the subject on the appropriate eCRF:

On a scale of 0 to 10, in which 0 is no pain and 10 is the worst possible or unbearable pain, please mark on the scale the number that best describes the pain or discomfort you are feeling in the operated eye at this time. The middle of the scale (around 5) can be used to describe "moderate pain". Only whole number scores are allowed.



Ocular pain status will be classified as "Absent" for a grade of 0 or "Present" for a grade of 1 to 10.

The efficacy variables will not be summarized. [redacted].

18. SAFETY ANALYSES

All safety analyses will be conducted using the Safety Set.

18.1 Adverse Events

An AE is defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not the event is considered drug-related. An AE can therefore be any unfavorable and unintended sign (e.g., an abnormal laboratory finding), symptom, or disease occurring after the subject started dosing with the study drug, without any judgment about causality. Any pre-existing medical condition that worsens after administration of the study drug will also be considered a new AE. Study drug includes the study drug under evaluation (OCS-01) and any comparator drug, vehicle, or any other medications required by the protocol given during any stage of the study. All AEs will be coded using MedDRA Version 26.1.

A TEAE is defined as any AE that occurs or worsens on or after the date of first dose of study medication.

Severity of an AE 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 assessment of severity is made irrespective of the relationship to study drug or the seriousness of the event and should be evaluated according to the following scale:

- Mild: AE is noticeable to the subject but is easily tolerated and does not interfere with the subject's daily activities.
- Moderate: AE is bothersome, possibly requiring additional therapy, and may interfere with the subject's daily activities.
- Severe: AE is intolerable, necessitates additional therapy or alteration of therapy, and interferes with the subject's daily activities.

The relationship of each AE to the study drug should be determined by the Investigator using these explanations:

- Suspected: A reasonable possibility exists that the study drug caused the AE.
- Not Suspected: A reasonable possibility does not exist that the study drug caused the AE.

Only TEAEs with a suspected relationship to the study drug are considered treatment-related TEAEs.

The expectedness of an AE should be determined based upon existing safety information about the study drug using these explanations:

- Unexpected: an AE that is not listed in the Investigator's Brochure (IB) or is not listed at the specificity or severity that has been observed.
- Expected: an AE that is listed in the IB at the specificity and severity that has been observed.

An AE is considered serious if, in the view of either the Investigator or Sponsor, it results in any of the following outcomes:

- Death

- A life-threatening AE
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- A congenital anomaly/birth defect

All summaries of expected and unexpected TEAEs will include only treatment-related TEAEs.

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 by actual treatment group. This summary will also include breakdowns of TEAEs further categorized as treatment-emergent serious adverse events (TE-SAEs), treatment-related TEAEs, treatment-related expected TEAEs, treatment-related unexpected TEAEs, TEAEs leading to study drug discontinuation, TEAEs leading to death, and TEAEs by maximum severity. Separate summaries will be created for all events, ocular events in study eyes, ocular events in fellow eyes, and non-ocular events.

TEAEs will be summarized using discrete summary statistics of subject and event numbers and presented by actual treatment group by SOC and PT for the following categories of TEAEs:

- Ocular TEAEs by SOC and PT
- Non-Ocular TEAEs by SOC and PT
- Ocular TE-SAEs by SOC and PT
- Non-Ocular TE-SAEs by SOC and PT
- Treatment-related Ocular TEAEs by SOC and PT
- Treatment-related Non-Ocular TEAEs by SOC and PT
- Treatment-related Expected Ocular TEAEs by SOC and PT
- Treatment-related Expected Non-Ocular TEAEs by SOC and PT
- Treatment-related Unexpected Ocular TEAEs by SOC and PT
- Treatment-related Unexpected Non-Ocular TEAEs by SOC and PT
- Ocular TEAEs by SOC, PT, and Maximum Severity
- Non-Ocular TEAEs by SOC, PT, and Maximum Severity

Ocular TEAEs will be summarized for study and fellow eyes separately. If a subject reports the same PT multiple times within the same SOC, that PT will only be reported once within that SOC. As with the PT, if a subject reports multiple conditions within the same SOC, that SOC will only be reported once. To count the number of subjects with any TEAEs by maximum severity, if a subject has multiple TEAEs coded to the same SOC or PT within an SOC, the subject will be counted once under the maximum severity for that SOC or PT. In the summary, SOCs will be listed in alphabetical order, and PTs within each SOC will be listed in order of descending frequency for the OCS-01 treatment group.

All AEs will be presented in a subject listing. In addition, all SAEs and AEs leading to study drug discontinuation will be presented in separate listings.

18.2 Pin-Hole Visual Acuity

Pin-hole VA is assessed at each visit using an ETDRS chart. Pin-hole VA testing will be done with a pin-hole occluder at a viewing distance of 4 meters at the beginning of each study visit (i.e., prior to slit lamp examination). If less than 20 letters are read at 4 meters the subject will perform the assessment again at a viewing distance of 1 meter. If at least 20 letters are read correctly at 4 meters, pin-hole VA is computed as 30 plus the number of letters correct at 4 meters. If less than 20 letters are read correctly at 4 meters, pin-hole VA is computed as the number of letters correct at 4 meters plus the number of letters correct at 1 meter.

For presentations in tables and listings, pin-hole VA will be converted from number of letters correct to a logarithm of the minimum angle of resolution (logMAR) score using the following formula:

logMAR VA = 1.70 – 0.02 * (Number of letters correct)

Summaries of pin-hole VA will be based on study eyes.

Pin-hole VA actual values at Visits 1, 2, 4, 5, 6, and 7 ([redacted] and change from baseline at Visits 4, 5, 6, and 7 ([redacted] will be summarized by visit and actual treatment group using continuous summary statistics.

Worsening of pin-hole visual acuity by at least 2 lines (10 letters) from the ETDRS scale from the previous visit at Visits 4, 5, 6, and 7 ([redacted] will be summarized by visit and actual treatment group using discrete summary statistics.

A subject listing of pinhole visual acuity by visit will be presented.

18.3 Intraocular Pressure

IOP in mmHg will be measured using a calibrated tonometer. Both eyes will be tested, with the right eye preceding the left eye. Two IOP measurements will initially be collected per eye. If the two IOP measurements differ by 2 mmHg or less, the mean of the two IOP measurements will be calculated and recorded as the final IOP measurement. If the two IOP measurements differ by more than 2 mmHg, a third (consecutive) IOP measurement will be collected and the median IOP measurement will be recorded as the final IOP measurement. For a given subject for a given eye, the dataset will have either the mean or median of the IOP measurements, but not both. The available measure will be used as the analysis value for IOP listings, summaries, and analyses.

Summaries of IOP will be based on study eyes.

IOP actual values at Visits 1, 2, 4, 5, 6, and 7 ([redacted] and change from baseline at Visits 4, 5, 6, and 7 ([redacted] will be summarized by visit and actual treatment group using continuous summary statistics.

Eyes with IOP of 30 mmHg or more at Visits 1, 2, 4, 5, 6, and 7 ([redacted] as well as eyes with an increase from baseline in IOP of 10 mmHg or more at Visits 4, 5, 6, and 7 ([redacted] will be summarized by visit and actual treatment group using discrete summary statistics. Percentages will be based on the number of subjects in each actual treatment group with responses.

A subject listing of IOP by visit will be presented.

18.4 Slit-Lamp Biomicroscopy Examination

A slit-lamp biomicroscopy examination of the eyelid, conjunctiva, cornea, anterior chamber, iris, and lens will be performed on the study eye at each visit except Visit 3 (and on both eyes at Visits 1 and 7 (The slit-lamp biomicroscopy examination results will be graded as normal, abnormal not clinically significant (NCS), or abnormal clinically significant (CS).

Summaries of slit-lamp biomicroscopy parameters will be based on study eyes.

The results for each region at Visits 1, 2, 4, 5, 6, and 7 (will be summarized by visit and actual treatment group using discrete summary statistics. Percentages will be based on the number of subjects in each actual treatment group with responses.

Shifts from baseline at Visits 4, 5, 6, and 7 (for the slit-lamp biomicroscopy parameters will be summarized by visit and actual treatment group using discrete summary statistics. Percentages for each visit will be based on the number of subjects in each actual treatment group with responses at both Visit 2 and the respective visit.

A subject listing of the slit-lamp biomicroscopy parameters will also be produced.

18.5 Dilated Indirect Ophthalmoscopy

A dilated indirect ophthalmoscopic examination of the vitreous, retina, macula, choroid, optic nerve, and lens will be performed at Visits 1 and 7 The results for each region will be graded as normal, abnormal NCS, and abnormal CS.

Summaries of dilated ophthalmoscopy parameters will be based on study eyes.

The results for each region at Visits 1 and 7 (will be summarized by visit and actual treatment group using discrete summary statistics. Percentages will be based on the number of subjects in each actual treatment group with responses.

Shifts from baseline at Visit 7 (for the dilated ophthalmoscopy parameters will be summarized by actual treatment group using discrete summary statistics. Percentages will be based on the number of subjects in each actual treatment group with responses at both Visits 1 and 7 ( ).

A subject listing of the dilated ophthalmoscopy parameters will also be produced.

18.6 Clinical Laboratory Data

Results from the urine pregnancy test at Visit 1 (will be provided in a subject listing.

19. INTERIM ANALYSES

Interim analyses will not be performed for this study.

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20. CHANGES FROM PROTOCOL-STATED ANALYSES

All efficacy analyses specified in the protocol and details pertaining to the efficacy analyses including statistical hypotheses, multiplicity adjustments, primary estimands, and handling of missing data for efficacy analyses as well as the PP set have been omitted from the ASAP [redacted]

21. 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. *Guidance for Industry: Submission of Abbreviated Reports and Synopses in Support of Marketing Applications*. U.S. Food and Drug Administration Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER). August 1999.

3. *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.

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22. PLANNED OUTPUT

22.1 Tables

Number	Title	Population
Table 14.1.1.1	Subject Disposition	
Table 14.1.1.2	Reasons for Screen Failures	Screen Failed Subjects
Table 14.1.2	Demographics	Safety Set
Table 14.1.3.1	Ocular Medical History	Safety Set
Table 14.1.3.2	Non-Ocular Medical History	Safety Set
Table 14.1.4.1	Ocular Concomitant Medications	Safety Set
Table 14.1.4.2	Non-Ocular Concomitant Medications	Safety Set
Table 14.1.4.3	Post-Baseline IOP-Lowering Medications by Visit	Safety Set
Table 14.3.1.1	Overall Summary of Treatment-Emergent Adverse Events	Safety Set
Table 14.3.1.2.1	Ocular Treatment-Emergent Adverse Events by System Organ Class and Preferred Term	Safety Set
Table 14.3.1.2.2	Non-Ocular TEAEs by System Organ Class and Preferred Term	Safety Set
Table 14.3.1.3.1	Ocular TE-SAEs by System Organ Class and Preferred Term	Safety Set
Table 14.3.1.3.2	Non-Ocular TE-SAEs by System Organ Class and Preferred Term	Safety Set
Table 14.3.1.4.1	Treatment-Related Ocular TEAEs by System Organ Class and Preferred Term	Safety Set
Table 14.3.1.4.2	Treatment-Related Non-Ocular TEAEs by System Organ Class and Preferred Term	Safety Set
Table 14.3.1.5.1	Treatment-Related Expected Ocular TEAEs by System Organ Class and Preferred Term	Safety Set
Table 14.3.1.5.2	Treatment-Related Expected Non-Ocular TEAEs by System Organ Class and Preferred Term	Safety Set
Table 14.3.1.6.1	Treatment-Related Unexpected Ocular TEAEs by System Organ Class and Preferred Term	Safety Set
Table 14.3.1.6.2	Treatment-Related Unexpected Non-Ocular TEAEs by System Organ Class and Preferred Term	Safety Set

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Number	Title	Population
Table 14.3.1.7.1	Ocular TEAEs by System Organ Class, Preferred Term, and Maximum Severity	Safety Set
Table 14.3.1.7.2	Non-Ocular TEAEs by System Organ Class, Preferred Term and Maximum Severity	Safety Set
Table 14.3.2	Pin-Hole Visual Acuity (logMAR) in Study Eyes by Visit	Safety Set
Table 14.3.3	Intraocular Pressure in Study Eyes by Visit	Safety Set
Table 14.3.4	Slit Lamp Biomicroscopy in Study Eyes by Visit	Safety Set
Table 14.3.5	Dilated Indirect Ophthalmoscopy in Study Eyes by Visit	Safety Set
Table 14.3.6	Treatment Exposure	Safety Set

22.2 Listings

Number	Title	Population
Listing 16.1.7	Randomization Schedule	All Randomized Subjects
Listing 16.2.1.1	Subject Disposition	All Randomized Subjects
Listing 16.2.2.1	Protocol Deviations	All Randomized Subjects
Listing 16.2.2.2	Inclusion/Exclusion Criteria	All Screened Subjects
Listing 16.2.3	Analysis Sets	All Randomized Subjects
Listing 16.2.4.1	Demographics	All Randomized Subjects
Listing 16.2.4.2.1	Ocular Medical History	All Randomized Subjects
Listing 16.2.4.2.2	Non-Ocular Medical History	All Randomized Subjects
Listing 16.2.4.3.1	Prior and Concomitant Ocular Medications	All Randomized Subjects
Listing 16.2.4.3.2	Prior and Concomitant Non-Ocular Medications	All Randomized Subjects
Listing 16.2.4.3.3	Prior and Concomitant IOP Lowering Medications	All Randomized Subjects
Listing 16.2.4.4	Concomitant Procedures	All Randomized Subjects
Listing 16.2.4.5	Cataract Surgery	All Randomized Subjects
Listing 16.2.5.1	Study Drug Assignment	All Randomized Subjects

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Number	Title	Population
Listing 16.2.5.2	Study Drug Administration	All Randomized Subjects
Listing 16.2.5.3	Study Drug Accountability	All Randomized Subjects
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]ed Subjects
Listing 16.2.7.1	Adverse Events	All Randomized Subjects
Listing 16.2.7.2	Serious Adverse Events	All Randomized Subjects
Listing 16.2.7.3	Adverse Events Leading to Study Drug Discontinuation	All Randomized Subjects
Listing 16.2.8	Urine Pregnancy Test - Subjects of Childbearing Potential	All Randomized Subjects
Listing 16.2.9.1	Pin-Hole Visual Acuity	All Randomized Subjects
Listing 16.2.9.2	Intraocular Pressure	All Randomized Subjects
Listing 16.2.9.3	Slit Lamp Biomicroscopy	All Randomized Subjects
Listing 16.2.9.4	Dilated Indirect Ophthalmoscopy	All Randomized Subjects

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23. APPENDICES

23.1 Appendix A

