STATISTICAL ANALYSIS PLAN

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

Sponsor: Oculis ehf.

Protocol Number: DX216

Author: [redacted]

SAP Version: 1.0 Final

SAP Date: 08-Nov-2019

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Statistical Analysis Plan Approval

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List of Abbreviations

ADaM	Analysis Data Model
AE	Adverse Event
ATC	Anatomical Therapeutic Chemical
BID	*Bis in die* (Twice Daily)
CI	Confidence Interval
CS	Clinically Significant
eCRF	Electronic Case Report Form
ETDRS	Early Treatment of Diabetic Retinopathy Study
FAS	Full Analysis Set
HIPAA	Health Insurance Portability and Accountability Act of 1996
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
IOP	Intraocular Pressure
LOCF	Last Observation Carried Forward
logMAR	Logarithm of the Minimum Angle of Resolution
MedDRA	Medical Dictionary for Regulatory Activities
MNAR	Missing Not at Random
NCS	Not Clinically Significant
OD	*Oculus Dexter* (Right Eye)
OS	*Oculus Sinister* (Left Eye)
OU	*Oculus Uterque* (Both Eyes)
PDF	Portable Document Format
PP	Per Protocol
PT	Preferred Term
QD	*Quaque die* (Once Daily)
RTF	Rich Text Format
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDC	Statistics & Data Corporation
SDTM	Study Data Tabulation Model
SOC	System Organ Class
TEAE	Treatment-Emergent Adverse Event
TLF	Tables, Listings, and Figures
WHO	World Health Organization

1. Introduction

The purpose of this statistical analysis plan (SAP) is to describe the planned analyses and reporting for protocol DX216, Amendment 1 dated 08-August-2019.

This SAP 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 and the most recent ICH E3 Guideline entitled Guidance for Industry: Structure and Content of Clinical Study Reports.

This SAP describes the data that will be analyzed and the subject characteristics, efficacy, and safety assessments that will be evaluated. This SAP provides details of the specific statistical methods that will be used. 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.

2. Study Objectives

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

The secondary objective of this study is to evaluate the optimal dosing frequency of OCS-01 (QD versus BID) in the treatment of inflammation and pain following cataract surgery.

2.1 Study Variables

2.2 Primary Variables

The hierarchical primary efficacy measures are the absence of anterior chamber cells [redacted] and the absence of pain [redacted]

2.3 Secondary Variables

The secondary efficacy measures include:

- Absence of anterior chamber cells [redacted]
- Absence of pain [redacted]
- Absence of flare [redacted]
- Absence of both anterior chamber cells and flare [redacted] and
- Use of rescue medication on or prior to each visit and overall.

2.4 Safety Variables

Safety variables to be summarized will include visual acuity, intraocular pressure (IOP), occurrence of adverse events (AE), and measurements from slit lamp biomicroscopy and dilated indirect ophthalmoscopy.

2.5 Statistical Hypotheses

The hierarchical statistical hypotheses for evaluating the objectives of the study are as follows:

Primary Endpoint:

[redacted]

Hierarchical Primary Endpoint:

[redacted]

Multiple comparison adjustments for testing OCS-01 BID and OCS-01 QD versus placebo (vehicle) in the absence of anterior chamber cells will not be made [redacted] A hierarchical testing strategy will be employed for testing absence of pain; statistical inference will only be made on the absence of pain endpoint if the corresponding OCS-01 dose (BID or QD) demonstrated statistical superiority over placebo (vehicle) in the absence of anterior chamber cells.

3. Study Design and Procedures

3.1 General Study Design

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

Eligible subjects will be randomized [redacted] to receive OCS-01 QD, OCS-01 BID, or placebo BID. Subjects will dose 1 drop in the study eye BID for 14 days, beginning 1 day post-surgery in the operated eye. The study will last 20-52 days, including screening and a follow-up visit at Visit 7 (Day 22 ± 2).

3.2 Schedule of Visits and Assessments

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

Table 1: Scheduled of Visits and Measurements

4. Study Treatments

Subjects will be assigned to 1 of 3 possible study treatments in this study. The study treatments to be evaluated in this study are:

- OCS-01 ophthalmic suspension (QD) + Placebo (vehicle) (QD)
- OCS-01 ophthalmic suspension (BID)
- Placebo (vehicle) ophthalmic suspension (BID)

[redacted].

4.1 Method of Assigning Subjects to Treatment Groups

Each subject who signs an informed consent form (ICF) will be assigned a screening number. Screening numbers will be assigned in sequential order at each site beginning with 001 and will follow the two-digit site number (e.g. subject 077 at Site 99 will have Screening Number 99-077). Inclusion and exclusion criteria will be reviewed, and qualifying subjects will be enrolled into the study. The screening number will be used to identify subjects in all datasets and listings for this study.

At the Visit 2 / Day 1 visit, eligible subjects will be randomized in a [redacted], stratified by site, to receive either OCS-01 ophthalmic suspension (QD) + Placebo (vehicle) (QD), OCS-01 ophthalmic suspension (BID), or Placebo (vehicle) ophthalmic suspension (BID).

4.2 Masking and Unmasking

An independent biostatistician who is not otherwise involved in the study will generate the final, unmasked subject randomization as well as the final, unmasked kit list randomization. Interactive response technology will be used to provide randomization assignments.

As described in Section 4, each subject will receive [redacted] Dosing boxes and pouches will be labeled this way regardless of whether the product within the [redacted] boxes is the same [redacted]

5. Sample Size and Power Considerations

With a total of [redacted] subjects [redacted], the study has [redacted] power to detect a statistically significant treatment difference between [redacted]

Additionally, with this sample size, the study has [redacted] power to detect a [redacted]

6. Data Preparation

6.1 Input Data

All reported study data will be recorded on the electronic case report forms (eCRF) supplied by Statistics & Data Corporation (SDC). Only the Principal Investigator and authorized study staff according to the Delegation of Responsibilities log are entitled to make entries in the eCRF.

After data are entered into the clinical study database, electronic edit checks and data review will be performed. All data validation specifications and procedures are detailed in the Data Validation Manual as a separate document. When the database has been declared to be complete and accurate, the database will be locked. Any changes to the database after data have been locked can only be made with the approval of the Sponsor and the clinical contract research organization (if applicable), in consultation with SDC.

All analyses outlined in this document will be carried out after the following have occurred:

- All data management requirements are met according to SDC standard operating procedures, including data entry, performance of edit and validation checks, documentation and resolution of data queries, and database lock with written authorization provided by appropriate SDC and Sponsor personnel.
- Protocol deviations have been identified and status defined (major/minor deviations).
- Analysis populations have been determined.
- Randomized treatment codes have been unmasked.

6.2 Output Data

Data from remote data capture and external data will be transferred to 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.

SDTM will follow the SDTM version 1.4 model and will be implemented using the SDTM Implementation Guide version 3.2 and the SDTM Controlled Terminology version 2016-06-24. ADaM data will follow the ADaM version 2.1 model and will be implemented using the ADaM Implementation Guide version 1.3. Both

SDTM and ADaM will be validated using Pinnacle 21 version 2.2. Any discrepancies in the validation will be noted in reviewer's guides accompanying the final data transfers.

Define.xml will be created for SDTM and ADaM using the Define-XML version 2.0 model

7. Analysis Populations

7.1 Enrolled Subjects Population

The enrolled subjects population will consist of [redacted]

7.2 Full Analysis Set

The full analysis set (FAS) will consist of al[redacted]

7.3 Per Protocol Population

The per protocol (PP) population is a [redacted]

7.4 Safety Population

The Safety population includes [redacted]

8. General Statistical Considerations

8.1 Unit of Analysis

For measurements taken at the subject level, the unit of analysis will be the individual subject and for measurements taken at the eye level, the unit of analysis will be the individual eye unless otherwise indicated. [redacted]

8.2 Missing or Inconclusive Data Handling

8.2.1 Partial Dates

Imputation of partial or missing dates will be conducted in order to classify 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:

- 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.
- 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 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 1 Jan of the same year as the end date.

Partial/missing end date:

- 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.
- 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 ongoing flag is missing or “Yes” then the date will not be imputed. If ongoing is “No” then the missing end date will be imputed as the last dose date.

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).

8.2.2 Missing Efficacy Data

The primary analyses of all efficacy data will use [redacted] to impute missing data; data for visits after a subject is discontinued for lack of efficacy or receives rescue medication will be imputed as failures for success/failure endpoints and will be imputed using [redacted] for other endpoints. Additional sensitivity analyses based on alternate handling of missing values will be conducted, and described in further detail in Section 13.1.1.

8.2.3 Missing Safety Data

For all safety variables, missing data will not be imputed, observed values will be presented.

8.3 Definition of Baseline

Baseline is defined as [redacted]

8.4 Data Analysis Conventions

All data analysis will be performed by SDC after the study is completed and the database has been locked. After the study database has been locked and any other prerequisites for unmasking are met (e.g. all protocol deviations have been classified as major or minor), unmasking will be done for the purpose of the primary analysis, and all planned tables, listings, and figures (TLF) will be generated.

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 TLF using landscape orientation. All study data will be listed by subject, treatment, and visit (as applicable) based on all randomized subjects unless otherwise specified (e.g. demography data, which is also captured for screen failure subjects).

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 groups and placebo (vehicle) will be calculated as active minus placebo and change from baseline will be calculated as follow-up visit minus baseline.

Dates within subject data listings will be presented based on ISO 8601 standard, as DD-MMM-YYYY.

All efficacy analyses will use a [redacted]

Unless otherwise specified, summaries will be presented by treatment group and (where applicable) eye and visit. Analysis by visit will be based on nominal visit identifier. Data from unscheduled visits, unscheduled time points, or unplanned repeat assessments will be included in the data listings. In general, these data will be excluded from the summary tables unless otherwise specified.

Efficacy summaries by treatment group will include the 3 protocol defined treatment groups. Summaries of subject disposition and baseline characteristics will include additional subject groupings defined as:

- [redacted]

[redacted]

For multiple imputation analyses where a seed may be specified, the seed will be set to 8-digit numeric value corresponding to the database lock date in YYYYMMDD format (eg, 20190901). If multiple seeds are needed within a program, the seed will be based on a 9-digit numeric consisting of the database lock date in YYYYMMDD format concatenated by an additional integer denoting the invocation number (eg, the first invocation would be 201909011, second would be 201909012). [redacted]

8.5 Adjustments for Multiplicity

The hierarchy of statistical hypotheses for testing is described in Section 2.5.

[redacted]

9. Disposition of Subjects

Disposition of subjects will be summarized for the [redacted]

Disposition of subjects will also be summarized among [redacted]

[redacted]

The number and percentage of subjects with major protocol deviations will be summarized by [redacted]

In addition, subject listings will be provided that include informed consent date, inclusion and exclusion criteria violations, and exclusions from the PP population.

Details of the study randomization, including randomization date and time, randomized treatment and actual treatment, will also be included within a subject listing.

10. Demographic and Pretreatment Variables

The demographic variables collected in this study include [redacted]

Age (years) will be summarized, overall and by treatment, using [redacted]

[redacted]

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

11. Medical History and Concomitant Medications

11.1 Medical History

Medical history and ocular history will be summarized [redacted]

Medical history and ocular history will be coded using Medical Dictionary for Regulatory Activities (MedDRA), version 22.0 (or higher).

Non-ocular medical history will be summarized [redacted]

Within table summaries, SOC will be listed in ascending alphabetical order; PTs will be listed in order of descending frequency for all subjects within each SOC.

Listings of medical history will be generated separately for ocular and non-ocular data. The study eye will be identified within listings of ocular medical history.

Details of each subject's cataract surgery will also listed.

11.2 Prior and Concomitant Medications

Prior and concomitant medication usage will be summarized with the [redacted]

Prior and concomitant medications will be coded using World Health Organization (WHO) Drug Global (B3, March 2019 [or higher]) dictionary, and summarized to the therapeutic drug class (Anatomical Therapeutic Chemical [ATC] Level 4 classification) and preferred name. If the ATC Level 4 classification is not provided, the next lowest 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. Any uncoded terms will be summarized under the ATC classification and preferred name of "Uncoded."

Prior medications are defined as [redacted] Concomitant medications are defined as [redacted]

Ocular medications are a subset of the overall medications and consist of those medication records where the location field on the eCRF is marked as OD, OS, or OU. In addition, medications which are classified as 'non-ocular' on the eCRF but which have potential to impact anterior chamber cell count or ocular pain will be reclassified as an ocular medication for analysis. These medications will be identified via manual review of coded medication classes as well as review of the indication fields. For purposes of analysis, the eye location value for analysis will be defined as OU.

IOP lowering medications are a subset of medications where the investigator has indicated on the eCRF that the medication was used to lower IOP. Concomitant medications will be summarized separately for ocular and non-ocular medications. [redacted]

[redacted] Medications reported as OU will be summarized as a medication for both the study eye as well as the non-study eye.

[redacted]

Listings of prior and concomitant medications will be generated separately for ocular and non-ocular data. A separate listing will be generated for IOP lowering medications.

Rescue medication usage is an efficacy measure for this study, analysis of rescue medication is described separately in Section 13.2.5.

12. Dosing Compliance and Treatment Exposure

12.1 Dosing Compliance

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.

12.2 Treatment Exposure

[redacted]

Although not captured directly on the CRF, 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 idenfied 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 (Day 15) 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 blinded data review will be conducted prior to database lock and unblinding 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.

[redacted]

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 Day 1. Details from the study drug accountability assessment will also be listed.

13. Efficacy Analyses

13.1 Primary Analysis

The hierarchical primary efficacy measures are the absence of anterior chamber cells [redacted] and the absence of pain [redacted]

The anterior chamber cell count will be recorded as t[redacted] Anterior chamber cell count is assessed for study eye only. Refer to **Table 2** for details.

Table 2. Anterior Chamber Cell Counts and Grade

[redacted]

Ocular pain will be assessed by the patient [redacted]

The observed anterior chamber cell count at Visit 6 will be used and categorized for analysis as follows:

- Absence of anterior chamber cells: [redacted]
- Presence of anterior chamber cells: [redacted]

Within this analysis, missing values for visits after a subject is discontinued for lack of efficacy or values obtained after subject has received rescue medication will be imputed as failures [redacted] for analysis. For all other missing data, LOCF will be used to impute the missing anterior chamber cell count grade, and the LOCF value will then be categorized for analysis as “cells present” or “cells absent”.

Derivation of the pain score and absence of pain [redacted] will follow the same approach for handling of missing data and handling of pain scores obtained following use of rescue medication.

The primary efficacy variables, the absence of anterior chamber cells at [redacted] and the absence of pain [redacted] will be summarized by [redacted]

For each OCS-01 dose (QD and BID) separately, the primary efficacy analyses will [redacted].

SAS® code used to generate the [redacted]

Comparison of OCS-01 QD versus placebo (vehicle) will be conducted in a similar manner, differing only by the treatment arms which are included within the comparison. Testing for each OCS-01 treatment group versus placebo (vehicle) for the absence of pain variable will use similar code.

[redacted]

Anterior chamber cell grade in the study eye at Visit 6 (Day 15) will be summarized by [redacted]

Ocular pain score at Visit 4 (Day 4) will be summarized by [redacted]

The primary efficacy analysis will be conducted using the FAS.

13.1.1 Sensitivity Analyses of the Primary Efficacy Measures

To check the robustness of primary efficacy analysis results, the previously described analyses of the primary efficacy measures will be repeated based on alternate handlings of missing data and major protocol deviations.

[redacted]

[redacted]

[redacted]

[redacted].

13.1.2 Subgroup Analyses of the Primary Efficacy Analysis

[redacted]

A blinded review of all medications will be conducted prior to database lock and unblinding in order to properly classify each subject into the appropriate category.

13.2 Secondary Analyses

The [redacted] will be used for the secondary analyses.

[redacted]

13.2.1 Anterior Chamber Cells

The anterior chamber cell grade at each visit and change from baseline / shift from baseline will be summarized by treatment group [redacted]

[redacted]

[redacted]

The observed anterior chamber cell grade values will be listed by subject and visit.

13.2.2 Ocular Pain

Absence of ocular pain at each visit will be summarized [redacted]

The observed ocular pain scores will be listed by subject and visit.

13.2.3 Anterior Chamber Flare

Anterior chamber flare is graded on a [redacted]

The observed anterior chamber flare grade values will be listed by subject and visit.

13.2.4 Absence of Both Anterior Chamber Cells and Flare

A composite variable based on absence of both anterior chamber cells and flare [redacted] will also be summarized.

[redacted]

13.2.5 Rescue Medication Usage

Rescue medications are defined for analysis as those concomitant medications where the eCRF question, [redacted] is answered [redacted]

[redacted]

[redacted]

Rescue medication will be listed by subject and medication.

14. Safety Analyses

All safety analyses will be conducted using the [redacted].

Analyses will be presented by treatment group. An additional "OCS-01 Total" group, consisting of all subjects in either OCS-01 treatment group, will also be included.

14.1 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. Treatment-emergent adverse events (TEAE) are defined as any event that occurs or worsens on or after the day and time when first treatment is initiated.

All AEs will be coded for analysis using MedDRA, version 22.0 (or higher).

Ocular AEs are a subset of AEs and are identified as those AEs where the location field on the AE eCRF is marked as OD, OS, or OU.

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 him/her by the subject. The assessment of severity is made irrespective of relationship to study drug or 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:

- *Supected*: 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.

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 classified as expected or not based on Investigator's assessment.

An overall summary will be presented that includes the number of TEAEs and the number and percentage of subjects who experienced at least one TEAE, by treatment group. This summary will include similar summaries of serious TEAEs, suspected treatment-related TEAEs, expected TEAEs, unexpected TEAEs, TEAEs leading to study drug discontinuation, TEAEs leading to death, and TEAEs by maximum severity. Results will be presented for all events (ocular and non-ocular) as well as separately for ocular and non-ocular events. Ocular events will be further separated into study eye versus non-study eye.

A summarization of non-ocular TEAEs will include the overall number of TEAEs and overall number and percentage of subjects who experienced at least one TEAE. The number of TEAEs and the number and percentage of subjects will also be tabulated by (primary) SOC and PT. Ocular TEAEs will be summarized in a similar manner, but with results further subdivided into study eye and non-study eye. Including the two above described analyses, summaries by SOC and PT will be provided for the following categories of AEs:

- Ocular TEAEs
- Non-ocular TEAEs
- Suspected treatment-related ocular TEAEs
- Suspected treatment-related non-ocular TEAEs
- Expected ocular TEAEs
- Expected non-ocular TEAEs
- Unexpected ocular TEAEs
- Unexpected non-ocular TEAEs
- Serious ocular TEAEs
- Serious non-ocular TEAEs

If a subject experiences the same PT multiple times within the same SOC, that subject will only be counted once for that PT witin that SOC. As with the PT, if a subject experiences multiple events within the same SOC, that subject will only be counted once for that SOC. In the summaries, SOC will be listed in ascending alphabetical order; PTs will be listed in order of descending frequency for all subjects within each SOC.

Summaries of TEAEs by maximum severity will be presented for ocular AEs (separately for treated eye and non-study eye) and non-ocular AEs separately. The number of subjects with any TEAEs (along with percentages) will be tabulated by SOC and PT within each SOC by treatment group, along with maximum severity per subject for each PT. To count the number of subjects with any TEAEs, if a subject has multiple

TEAEs coded to the same PT within the same SOC, the subject will be counted once under the maximum severity.

Separate listings of AEs will be produced to list all AEs, AEs leading to study drug discontinuation, and serious AEs. TEAEs will be identified within the listings.

14.2 Pin-hole Visual Acuity

Pin-hole, logarithm of the minimum angle of resolution (logMAR) visual acuity is assessed [redacted]

[redacted]

[redacted].

[redacted]

14.3 Slit-Lamp Biomicroscopy Examination

A slit-lamp biomicroscopy examination of the eyelid, conjunctiva, cornea, anterior chamber, iris, and lens will be performed [redacted] The results will be graded as normal, abnormal not clinically significant (NCS), or abnormal clinically significant (CS).

[redacted]

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

14.4 Dilated Indirect Ophthalmoscopy

A dilated indirect ophthalmoscopy examination of the vitreous, retina, macula, choroid, and optic nerve will be performed at [redacted] The results will be graded as normal, abnormal NCS, or abnormal CS.

[redacted]

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

14.5 Intraocular Pressure (IOP)

Subjects' IOP will be assessed in each eye [redacted]

Analyses of concomitant IOP lowering medications is described previously, within Section 11.2.

14.6 Clinical Laboratory Data

Results from the urine pregnancy test at Visit 1 (Day -28 to -1) and Visit 7 (Day 22) will be listed by subject.

15. Interim Analyses

Interim analyses will not be performed.

16. Changes from Protocol-Stated Analyses

There are no changes from the protocol-stated analyses.

17. References

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Ratich, B., Lipkovich, I., Kelly, M., Combining Analysis Results from Mulitply Imputed Categorical Data. PharmaSUG 2013 – Paper SP03, 2013.

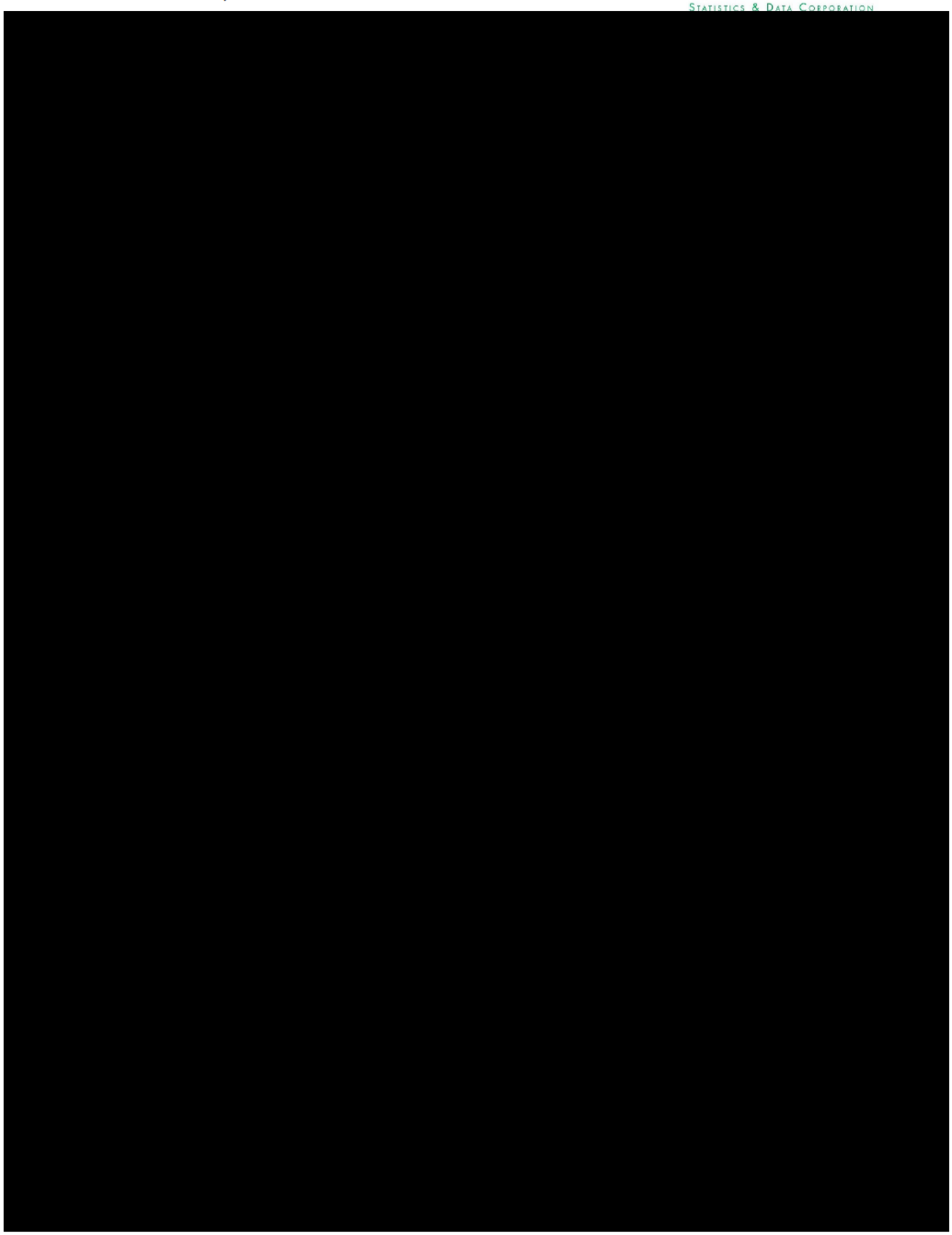
Wilson, E. B., Hilferty, M. M. The distribution of chi-square. *Proceedings of the National Academy of Sciences of the United States of America*, 17, 684-688. 1931.

18. Revision History

Documentation of revision to the SAP will commence after approval of the final version 1.0.

19. Tables

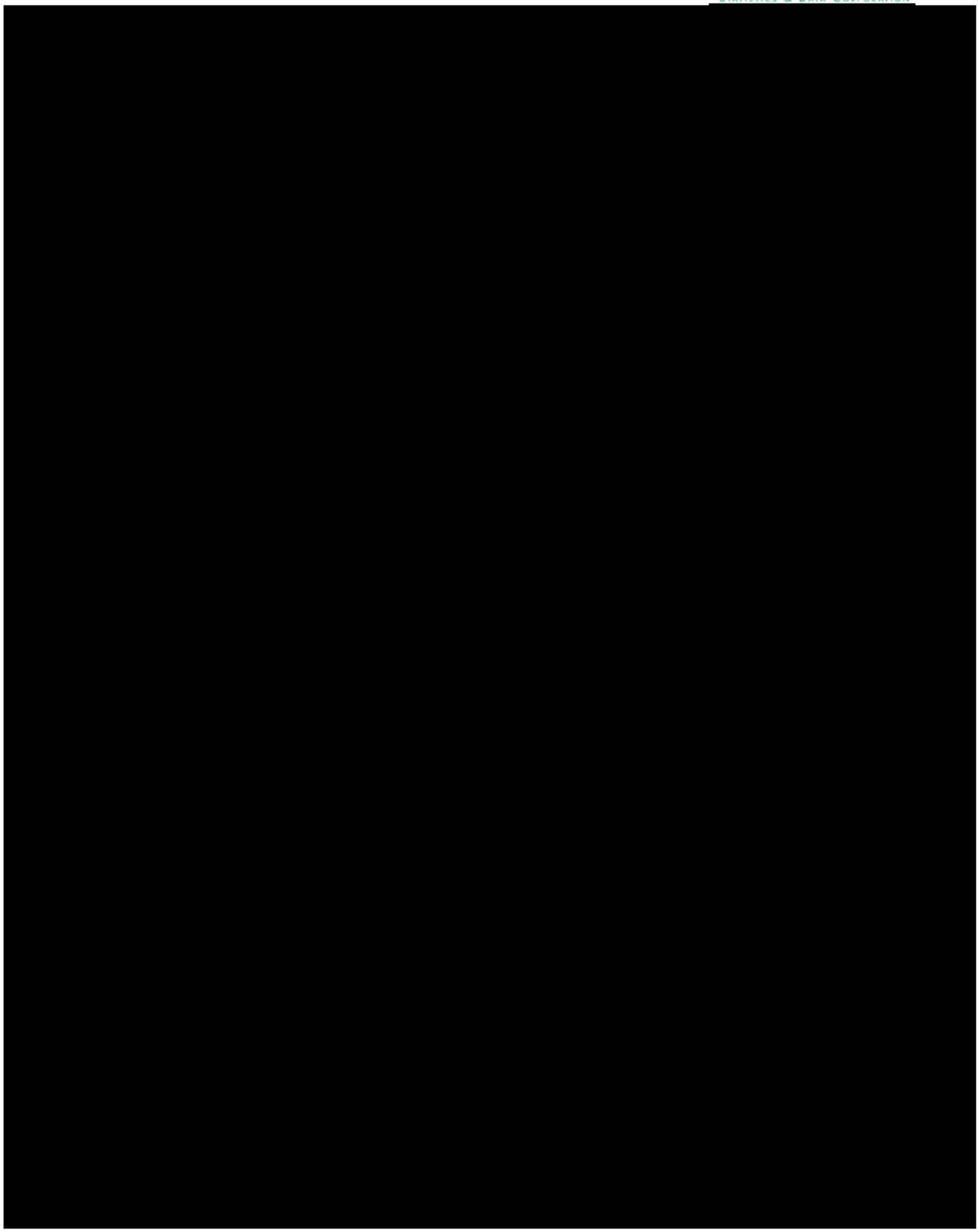
Tables that will be included in the topline delivery are shown in boldface font.



[redacted]

20. Listings

[redacted]



21. Figures