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Statistical Analysis Plan

SPONSOR:	Aura Biosciences, Inc.
PROTOCOL TITLE:	**A Phase 1b/2 Open-label, Ascending Single and Repeat Dose Clinical Trial Designed to Evaluate the safety and efficacy of Light-activated AU-011 for the Treatment of Subjects with Small Primary Choroidal Melanoma** **NCT03052127**
STUDY CODE:	AU-011-101

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1 List of Abbreviations and Definition of Terms

Abbreviation	Term
A-scan	A-scan ultrasonography
ADA	Anti-Drug Antibodies
AE	Adverse Event
ALT	Alanine Aminotransferase
AST	Aspartate Transaminase
ATC	Anatomical Therapeutic Chemical
AU-011	A modified human papillomavirus-derived, empty viral like particle (VLP) conjugated to approximately 200 molecules of photosensitizer IRDye® 700DX
B-scan	B-scan ultrasonography
BCVA	Best Corrected Visual Acuity
BP	Blood Pressure
BUN	Blood Urea Nitrogen
CBC	Complete Blood Count
CK	Creatine Kinase
CM	Choroidal Melanoma
CMP	Comprehensive Metabolic Panel
CTC	Common Toxicity Criteria
DG	Documented Growth
DLT	Dose Limiting Toxicity
DP	Disease Progression
eCRF	Electronic Case Report Form
EDI-OCT	Enhanced Depth Imaging Optical Coherence Tomography
ETDRS	Early Treatment Diabetic Retinopathy Study
FA	Fluorescein Angiography
GGT	Gamma-Glutamyltransferase
ICH	International Conference on Harmonization
IOP	Intraocular Pressure
ITT	Intention-To-Treat
IVT	Intravitreal
LBD	Largest Basal Diameter
LDH	Lactate Dehydrogenase
LLN	Lower limit of normal
LOCF	Last Observation Carried Forawrd
MAD	Multiple Ascending Dose
MCV	Mean Corpuscular Volume
MedDRA	Medical Dictionary for Regulatory Activities

Min	Minute
mmHG	Millimeter of Mercury
µg	Microgram
µL	Microliter
n	Number of non-missing values
NCI	National Cancer Institute
NCI-CTC	National Center Institute - Common Terminology Criteria
nm	Nanometer
OCTA	Optical Coherence Tomography Angiography
OD	Right eye
OS	Left eye
OU	Both eyes
PR	Partial Response
PSC	Posterior Subcapsular Cataract
PT	Preferred Term
RBC	Red Blood Cells
SAD	Single Ascending Dose
SAE	Serious Adverse Event
SAF	Safety
SAP	Statistical Analysis Plan
SD	Stable Disease
SGOT	Serum Glucose-Oxaloacetic Transaminase
SGPT	Serum Glucose-Pyruvic Transaminase
SOC	System Organ Class
TE	Treatment-Emergent
TEAE	Treatment-Emergent Adverse Event
ULN	Upper limit of normal
WBC	White Blood Cells
WHO	World Health Organization

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2 Introduction

This original Statistical Analysis Plan (SAP) V1.0 was written for Study AU-011-101 conducted in subjects with small to medium primary choroidal melanoma on the basis of Clinical Protocol Rev-7, 25 May 2018. The International Conference on Harmonization (ICH) guideline E3 "Structure and Content of Clinical Study Reports" was used as a guide to the writing of the plan.

The revision of the SAP was made on the basis of Clinical Protocol Protocol Rev-15, 21 Feb. 2020.

An overview of the changes made in the SAP v2.0:

- Revision of primary objective and secondary objectives.
- Addition of Expansion cohort (Cohort 9), Observational cohort (Cohort 10), and 2 Cycles of AU-011 cohorts (Cohort 11 and Cohort 12)
- The 2nd Interim Analysis was decided to be cancelled.
- Number of subjects in the study increased from 45 to 60.
- Number of study sites in the study increased from 10 to 15.
- Addition of the definitions of subgroups, and subgroup analyses.
- Revision of the definitions of Tumor control, Partial response and disease progression.
- Addition of tumor growth rate analysis.
- The final analysis would be performed after all subjects complete the Week 52 Visit.

An overview of the changes made in the SAP v3.0:

- Revision of tumor response assessment to consider various factors that could have impacted the determination of tumor response.
- Addition of a new analysis population: Efficacy Evaluable population, to exclude subjects from site 009 due to significant GCP deviations.
- Addition of analyses of ocular TEAEs related study drug/injection procedure/laser.

An overview of the changes made in the SAP v4.0:

- Redefined the ITT population (instead of the Efficacy Evaluable population) as the primary population for efficacy analysis.
- Revision of the criteria for subjects with an AE of pigmentary changes in the determination of tumor response.
- Addition of analyses of tumor response and visual acuity for site 009 subjects only.
- Addition of analyses of subjects with visual acuity preservation.

An overview of the changes made in the SAP v5.0 (after the 1st DB lock on 25 Aug. 2021):

- More details/clarification of rules given specifically for tumor response analysis at Month 12 LOCF and Last Visit.
- Revision of the criteria for visual acuity failure for consistency with the overall definition when data are not available at both Week 39 and Week 52.

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3 Study Design and Objectives

3.1 Study Objectives

3.1.1 Primary Objective

The primary objective of this study is to evaluate the safety of IVT administration of one of 3 dose levels, repeat dose regimens and one or two laser applications of Light-activated AU-011 given in one or two treatment cycles in the treatment of subjects with small primary choroidal melanoma.

3.1.2 Secondary Objectives

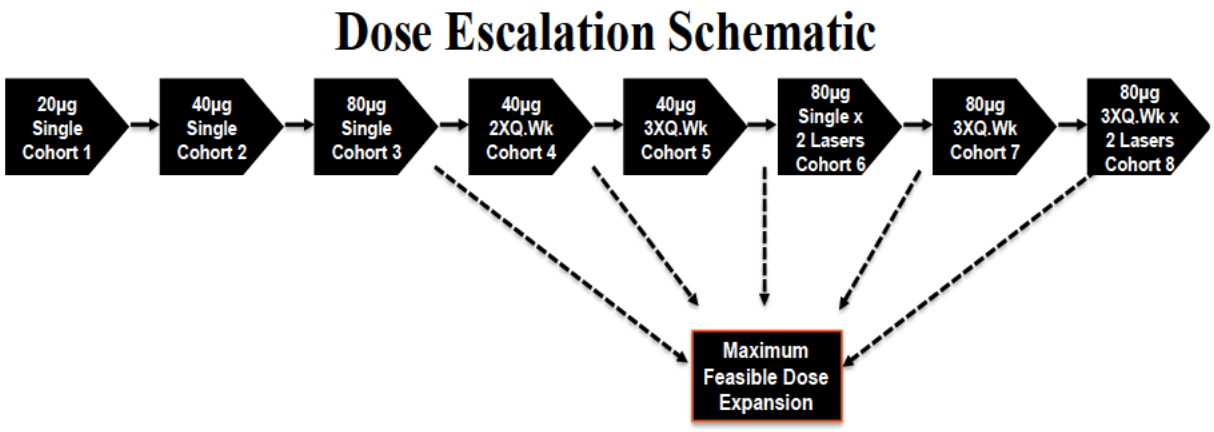
Secondary objectives include evaluating:

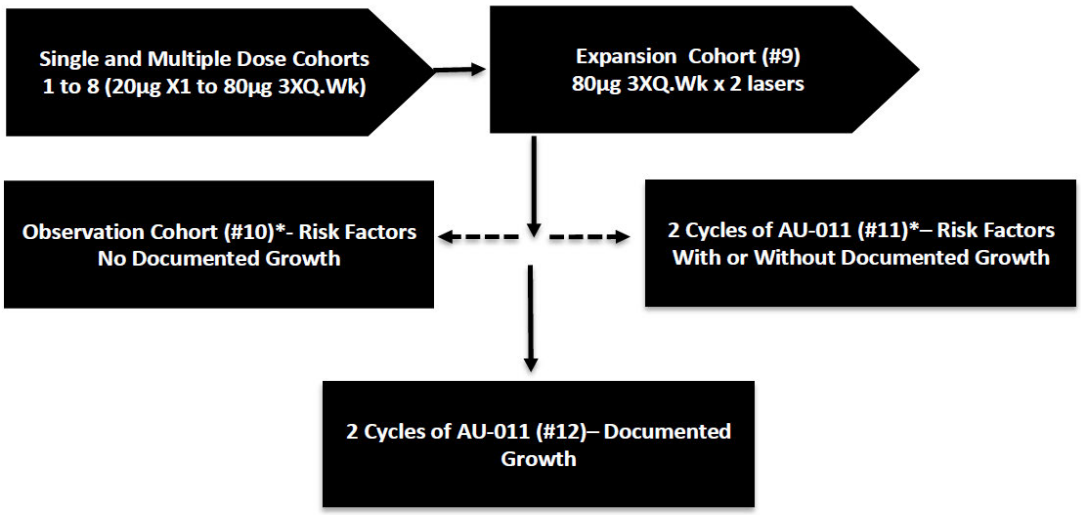
- Efficacy of AU-011 with one or two treatment cycles with the maximum safe and feasible dose
- Efficacy and safety of AU-011 in subjects with documented growth
- The immunogenicity of AU-011
- A-scan amplitudes of the internal reflectivity of the lesion at study sites with diagnostic probes
- Optical coherence tomography angiography (OCTA) image changes at study sites with OCTA imaging systems for Cohorts 6 through 9

3.2 Study Design

This is an open-label, ascending single and repeat dose and cycle, multicenter study, designed to evaluate the safety and efficacy of Light-activated AU-011 at 3 dose levels and repeat dose regimens and cycles of Light-activated AU-011 and one or two laser applications in subjects with small primary choroidal melanoma (CM). The dose escalation design is shown in the figure below.

Figure 1 Dose Escalation Schematic





**Alternating enrollment Cohort 10 & 11 will be closed with this revision(Rev-11) and subjects will be enrolled in Cohort 12.*

Single Ascending Dose (SAD) Cohorts

Three subjects will receive a single intravitreal (IVT) injection of Light-activated AU-011 low dose (20 µg in [redacted] µL). The injection is followed 6 to 8 hours later by exposure to 689 nm laser light. No more than one subject may be treated per day, and the treated subject must complete his/her 24-hour post-treatment visit with no safety issues before the next subject in a given cohort may be treated.

If all 3 subjects in the low dose group complete treatment without any dose limiting toxicity (DLT), escalation to the medium dose level (40 µg in [redacted] µL) group will be initiated. If a DLT is observed in 1 subject in the low dose group, this group will be expanded to 6 subjects. Dose escalation will not be allowed if 2 or more subjects in the low dose group experience a treatment-related DLT. Instead, if 2 or more subjects in the low dose group experience a treatment-related DLT, dose reduction to 10 µg in [redacted] µL may be considered for enrolling an additional 3 subjects.

One week after the last subject in the low dose group completes treatment, the study medical monitor and independent ocular oncologist will review safety data for all subjects in the low dose group. After review and confirmation that the data support proceeding to treatment with the medium dose group, three subjects will receive a single IVT injection of Light-activated AU-011 medium dose (40 µg in [redacted] µL). The injection is followed 6 to 8 hours later by exposure to 689 nm laser light.

If all 3 subjects in the medium dose group complete treatment without any dose limiting toxicity (DLT), escalation to the high dose level group will be initiated. If a DLT is observed in 1 subject in the medium dose group, this group will be expanded to 6 subjects. If 2 or more subjects in the medium dose group experience a DLT after their treatment, this will confirm that the low dose level is the maximum feasible dose (due to formulation limits).

One week after the last subject in the medium dose group completes treatment, the study medical monitor and an independent ocular oncologist will review safety data for all subjects in the medium dose group. After review and confirmation that the data support proceeding to treatment with the high dose group, three subjects will receive a single dose of Light-activated AU-011 high dose (80 µg administered as 2 injections of 40 µg in [redacted] µL not more than two hours apart). The second injection is followed 6 to 8 hours later by exposure to 689 nm laser light. If a DLT is observed in 1 subject in the high dose group, this group will be expanded to 6 subjects. If 2 or more subjects in the high dose group

experience a DLT after their treatment, this will confirm that the medium dose level is the maximum feasible dose and the dose chosen for the repeat dose phase of the study will drop to one dose below the maximum feasible dose of 40 µg and the lower dose of 20 µg will be given as repeat doses.

Multiple Ascending Dose (MAD) Cohorts

One day after the last subject in the high dose group completes treatment, the study medical monitor and independent ocular oncologist will review safety data for all subjects and recommend proceeding to the repeat dose phase of the study. After review and confirmation that the data support proceeding to repeat dose regimens, 3 subjects will receive an IVT injection of 40 µg in [redacted] µL of Light-activated AU 011 as 2 repeat doses 1 week apart. Each injection is followed 6 to 8 hours later by exposure to 689 nm laser light.

If all 3 subjects in this 2 repeat 40 µg dose group complete treatment without any dose limiting toxicity (DLT) after 2 injections, then this regimen may be investigated further in subsequent studies. If a DLT is observed in 1 subject in this 2 repeat 40 µg dose group, this group will be expanded to 6 subjects. If 2 or more subjects in this 2 repeat 40 µg dose group experience a DLT after their treatment, this will confirm that a lower repeat dose regimen should be investigated.

One day after the last subject in the 2 repeat 40 µg dose group completes treatment, the study medical monitor and independent ocular oncologist will review safety data for all subjects and identify whether it is safe to evaluate 3 repeat 40 µg doses in the next cohort of the study.

After review and confirmation that the data support proceeding to a 3 repeat 40 µg dose regimen, 3 subjects will receive an IVT injection of 40 µg in [redacted] µL of Light-activated AU-011 as 3 repeat doses 1 week apart. Each injection is followed 6 to 8 hours later by exposure to 689 nm laser light.

If all 3 subjects in this 3 repeat 40 µg dose group complete treatment without any dose limiting toxicity (DLT) after 3 injections, escalation to the next dose cohort will be initiated. If a DLT is observed in 1 subject in this 3 repeat 40 µg dose group, this group will be expanded to 6 subjects. If 2 or more subjects in this 3 repeat 40 µg dose group experience a DLT after their treatment, this will confirm that a fewer number of repeat administrations, or a lower dose at each administration should be investigated.

One day after the last subject in the 3 repeat 40 µg dose group completes treatment, the study medical monitor and independent ocular oncologist will review safety data for all subjects and identify the maximum feasible dose for continued evaluation in the repeat dose phase of the study. After review and confirmation that the data support proceeding, an 80 µg single dose repeat laser regimen will be initiated. Three subjects will receive IVT administration of 80 µg of Light-activated AU-011 administered as 2 injections of 40 µg in [redacted] µL (not more than 2 hours apart) followed by two 689 nm laser applications 30 minutes (± 10 minutes) apart, with the first of the 2 laser applications occurring 6 to 8 hours after the second injection.

If all 3 subjects in this 80 µg single dose followed by 2 laser applications dose group complete treatment without any dose limiting toxicity (DLT), then the study may progress to the next cohort. If a DLT is observed in 1 subject in this 2 repeat laser applications following 80 µg single dose group, this group will be expanded to 6 subjects. If 2 or more subjects in this 2 repeat laser applications following 80 µg single dose group experience a DLT after their treatment, this will confirm that a lower dose followed by repeat laser regimen, or a repeat dose followed by single laser application, should be investigated further.

One day after the last subject in the 2 repeat laser applications following 80 µg single dose group completes treatment, the study medical monitor and independent ocular oncologist

will review safety data for all subjects and identify whether it is safe to evaluate repeat laser applications after each of 3 repeat doses of 80 µg in the study.

After review and confirmation that the data support proceeding to the 3 repeat 80 µg dose regimen followed by a single laser application, 3 subjects will receive an IVT administration of 80 µg of Light-activated AU-011 administered as 2 injections of 40 µg in [redacted] µL (not more than 2 hours apart) as 3 repeat doses one week apart. Each administration is followed 6 to 8 hours (after the second injection) later by exposure to 689 nm laser light.

One day after the last subject in the 3 repeat 80 µg dose group, followed by a single laser application, completes treatment and 4 weeks after the last subject in the 80 µg single dose followed by 2 laser applications dose group complete treatment, the study medical monitor and independent ocular oncologist will review safety data for all subjects and identify whether it is safe to evaluate 3 repeat doses of 80 µg, each followed by 2 repeat laser applications, in the next cohort of the study.

After review and confirmation that the data support proceeding to repeat laser applications after each of 3 repeat 80 µg doses, 3 subjects will receive an IVT administration of 80 µg of Light-activated AU-011 administered as 2 injections of 40 µg in [redacted] µL (not more than 2 hours apart) as 3 repeat doses one week apart. Each administration is followed 6 to 8 hours (after the second injection) later by 2 exposures to 689 nm laser light 30 minutes (± 10 minutes) apart.

If all 3 subjects in this group, who receive 3 repeat 80 µg doses, each followed by 2 repeat laser applications, complete treatment and have been followed for 4 weeks without any dose limiting toxicity (DLT) after 3 weekly administrations, then this dose and regimen will be considered the maximum feasible dose and investigated in the expanded cohort. If a DLT is observed in 1 subject in this 3 repeat 80 µg dose with 2 repeat laser applications group, this group will be expanded to 6 subjects. If 2 or more subjects in this 3 repeat 80 µg dose with 2 repeat laser applications group experience a DLT after their treatment, this will confirm that a fewer number of repeat administrations of either Light-activated AU-011 or laser, or both, or a lower dose of Light-activated AU-011 at each administration should be investigated further.

Four weeks after the final treatment of the final subject in this cohort, a review of the safety data (including EDI-OCT) by the study medical monitor and independent ocular oncologist will occur. If safety is confirmed, the 3 repeat 80 µg dose with 2 repeat laser applications will be considered the maximum feasible and tolerated dose and this regimen will be expanded by up to 12 additional subjects in Cohort 9.

Repeat Cycle and Observation Cohorts

Once the last subject in the expansion cohort has been enrolled and safety of the maximum safe and feasible dose is confirmed, approximately 6 additional subjects, who fulfil the criteria for the clinical diagnosis of CM, but without documented growth, will be enrolled into an observation cohort (Cohort 10). These subjects will be assessed every 3 months (ie, 90 day (+/- 7 days) intervals from the Screening Visit) until tumor growth of the CM lesion is established (as defined in Protocol Section 8.3.4.) and at which time will then receive treatment with AU-011, as 3 repeat 80 µg doses, each followed by 2 repeat laser applications and move to the same visit schedule as subjects entering the trial and receiving treatment with AU-011 immediately. These subjects will receive Cycle 2 of AU-011 administered as 3 repeat 80 µg doses, each followed by 2 repeat laser applications no earlier than the Week 12 Visit and after resolution of any inflammation resulting from the first cycle or when the inflammation is minimal and decreasing based on investigator judgement. Cycle 2 should be administered as soon as reasonably possible after inflammation has resolved or is minimal and decreasing based on investigator judgement.

In addition, approximately 6 additional subjects, who meet the criteria for a clinical diagnosis of CM, with or without documented growth, will enter Cohort 11 and receive two cycles of AU-011 treatment (each cycle will be comprised of 3 repeat 80 µg doses, each followed by 2 repeat laser applications). Cycle 2 of AU-011 will be administered as 3 repeat 80 µg doses, each followed by 2 repeat laser applications no earlier than the Week 12 Visit and after resolution of any inflammation resulting from the first cycle or when the inflammation is minimal and decreasing based on investigator judgement. Cycle 2 should be administered as soon as reasonably possible after inflammation has resolved or is minimal and decreasing based on investigator judgement.

The intention is to alternate the enrolment of Cohorts 10 and 11. If during the enrollment of these subjects, a subject has just been enrolled into Cohort 11 and a subject with documented growth presents, then that subject may instead be enrolled into Cohort 11 rather than Cohort 10 for which they would not be eligible due the to the presence of documented growth and instead will be assigned to receive the first of 2 cycles of AU-011.

If 2 subjects experience a DLT during treatment with Cycle 2, then no further subjects will receive Cycle 2 of AU-011 until discussed with the independent ocular oncologist and medical monitor and continuation of enrollment is confirmed.

Subjects with Documented Growth

Enrollment in Cohorts 10 and 11 was closed following approval of protocol revision 11 (Rev-11) at each site. An additional cohort, Cohort 12, of subjects with minimum defined levels of documented growth will be initiated to allow assessment of safety and efficacy of 2 cycles of AU-011 treatment in this key subgroup of subjects with CM. Since Cohort 12 has the same dose as Cohort 11, no additional safety review will be required prior to initiating this cohort.

Up to 15 subjects, who meet the criteria for a clinical diagnosis of CM with documented growth (as defined in Protocol Inclusion Criteria 5C) will enter Cohort 12 and receive two cycles of AU-011 treatment (each cycle will be comprised of 3 repeat 80 µg doses, each followed by 2 repeat laser applications). Cycle 2 of AU-011 will be administered as 3 repeat 80 µg doses, each followed by 2 repeat laser applications no earlier than the Week 12 Visit and after resolution of any inflammation resulting from the first cycle or when the inflammation is minimal and decreasing based on investigator judgement. Cycle 2 should be administered as soon as reasonably possible after inflammation has resolved or is minimal and decreasing based on investigator judgement.

If 2 subjects experience a DLT during treatment with Cycle 2, then no further subjects will receive Cycle 2 of AU-011 until discussed with the independent ocular oncologist and medical monitor and continuation of enrollment is confirmed.

3.3 Sample Size Justification

No formal sample size calculation was performed for this ascending single and repeat dose and cycle phase 1b/2 study. Approximately 60 subjects with small primary CM will be enrolled and treated with Light-activated AU-011 at 3 dose levels and repeat dose regimens and cycles of Light-activated AU-011 and one or two laser applications.

The study was designed to investigate at least 3 subjects at each treatment level and expand to investigate an additional 6 subjects at the maximum feasible dose. Provisions for expanding cohorts based on observed DLTs were also provided as per the study design section above.

4 General Analysis Definitions

Data will be analyzed using SAS (Version 9.4 or later).

No tests of significance will be carried out to compare cohorts on baseline data because any observed differences between them must be attributed to chance.

Since this is an exploratory study, no formal hypothesis testing will be performed. Descriptive statistics will be used to tabulate and summarize baseline, efficacy and safety outcomes.

Descriptive statistics will be tabulated as follows:

- Categorical data will be summarized in contingency tables presenting frequencies and percentages.
- Continuous data will be summarized using number of non-missing values (n), mean, standard deviation, median, minimum and maximum values.

The tables will be created by cohort and overall, in the order as listed in Section 4.5.4. In addition, a subtotal of dose escalation cohorts (Cohort 1 to 8) and a subtotal of the expansion cohorts (Cohort 9 to 12) will be included in all the relevant tables.

Listings with individual values will be provided for all data presented in the tables.

4.1 Study Period and Visit Window Definitions

4.1.1 Study Periods

The study consists of 3 periods: screening, active period and follow-up period. Results will be presented by visit and not by period.

4.1.2 Visit Windows

The schedule of study assessments can be found in Appendix 11.1 of this SAP.

Missing scheduled visit will be substituted by an unscheduled or early withdrawal visit occurring within each follow-up visit window. If there are multiple unscheduled or early withdrawal visits occurring within the window, the closest one within the visit window will be used. If no unscheduled or early withdrawal visit occurred within the window, the visit will be considered as missing. The details are tabulated in Appendix 11.2.

An exception to this visit-window algorithm is the analysis of the "Last Visit". For all "Last Visit" time-point analyses, a subject's last non-missing endpoint assessment will be used for the analysis, regardless of if the visit falls within a particular visit window or not.

4.2 Planned analyses

Two interim analyses are planned: 1) after the first 2 cohorts (SAD cohorts) have completed 12 months of follow-up (Visit 14); and 2) after all subjects complete Week 12 visit (Visit 11).

The final analysis will be performed when all enrolled subjects will have completed the End of Study visit or the Early Termination visit, if early discontinued from study.

Note on SAP V2.0:

1) One interim analysis was performed for the '01AUG2018 Deliverable".
2) No further interim analyses are going to be done.
3) Due to the early termination of the study, the final analysis will be performed after all subjects complete the Week 52 Visit.

4.3 Definition of Populations

4.3.1 Intention-To-Treat Population

The Intention-To-Treat (ITT) population will consist of all enrolled subjects, whether or not they receive one administration of study treatment.

This is the primary population for the efficacy analysis.

4.3.2 Efficacy Evaluable Population

The Efficacy Evaluable population will consist of ITT population subjects, excluding subjects from site 009, who have been excluded based on site audit findings.

This population will be used as a sensitivity analysis for efficacy.

4.3.3 Safety Population

The Safety population will include all subjects who received at least one administration of study treatment. Subjects will be analyzed according to the treatment that they actually received.

This is the primary population for the safety analysis.

4.4 Subgroup Definitions

The following subgroups are defined for additional characterization of efficacy and/or safety of AU-011:

- Subjects with documented growth (DG): defined as subjects who had any amount of documented growth on tumor thickness
- Phase 3 Eligible (Ph3 Elig): defined as subjects with entry criteria similar to planned phase 3 critieria
  - Subjects with tumor thickness of ≥0.5 mm and ≤3.0 mm on B-scan ultrasound, a largest basal diameter of ≤13.0 mm on fundus photos with an estimated tumor volume ≤50 mm^3 and tumor growth of ≥0.3 mm on tumor thickness within 2 years of screening
- Phase 3 Eligible Therapeutic Regimen at 2 cycles (Ph3 Elig TR2C)
  - Phase 3 Eligible subjects who received 2 cycles of AU-011 treatment, each cycle comprised of three weekly treatments with 80µg x 2 laser applications
- Phase 3 Eligible - High Risk for Vision Loss (Ph3 Elig HRVL)
  - Phase 3 Eligible subjects with tumor ≤3.0 mm from the fovea or optic disc

4.5 Treatment Assignment and Treatment Cohorts

4.5.1 Description of Study Drug

Light-activated AU-011 is a combination product consisting of a drug (AU-011) and a laser (Aura Photoactivation system) that delivers 689 nm light to activate the drug once it is bound to the tumor cells. AU-011 drug substance is a modified human papillomavirus-derived, empty viral like particle (VLP) conjugated to approximately 200 molecules of a phthalocyanine-based photosensitizer IRDye®700DX. AU-011 drug product is a sterile, pale blue aqueous solution supplied at a concentration of 0.4 mg per mL of buffered isotonic solution (pH 6.5). AU-011 is supplied in a [redacted] mL, high density plastic, single-use vial; each vial contains a fill volume of [redacted] mL.

4.5.2 Administration of AU-011

In this clinical trial, AU-011 study drug will be administered by IVT injection and will be followed by laser light application (689 nm) to the CM 6 to 8 hours after administration of AU-011. The maximum concentration of the current AU-011 formulation is 40 µg in [redacted] µl and as a result, the maximum feasible dose is 80 µg administered as [redacted] injections of 40µg in [redacted] µl.

AU-011 will be administered via IVT injection as a low dose (20 µg) per IVT injection ([redacted] µL injection), a medium dose (40 µg) per IVT injection ([redacted] µL injection), or a high dose (80 µg) per IVT injection ([redacted] µL injections with interim IOP assessment).

Subjects in cohorts 1 (20 µg single dose), 2 (40 µg single dose) and 3 (80 µg single administration given as [redacted] injections of 40 µg in [redacted]µl) will receive one treatment followed by a single laser application, subjects in cohort 4 (40 µg two repeat doses) will receive [redacted] injections one week apart followed by a single laser application, subjects in cohort 5 (40 µg three repeat doses) will receive [redacted] injections one week apart followed by a single laser application, subjects in cohort 6 (80 µg single dose followed by 2 laser applications) will receive a single dose administered as [redacted] injections of 40 µg in [redacted] µl followed by 2 laser applications, subjects in cohort 7 (80 µg three repeat doses followed by a single laser application) will receive 3 doses each administered as [redacted] injections of 40 µg in [redacted] µl one week apart followed by a single laser application, and subjects in cohorts 8 and 9 (80 µg three repeat doses followed by two laser applications) will receive 3 doses each administered as [redacted] injections of 40 µg in [redacted] µl one week apart followed by 2 laser applications. Subjects in cohorts 3, 6, 7, 8 and 9 receiving 80 µg doses given as [redacted] injections of 40 µg in [redacted] µl will have their IOP measured prior to and after each injection. IOP must be 21 mm Hg or less before each injection can be given and the maximum interval between the two injections is 2 hours. IOP must also be 21 mm Hg or less before the subject is discharged from the clinic.

Subjects enrolled in the observation cohort and after exhibiting tumor growth (Cohort 10), and repeat cycle cohorts (Cohorts 11 and 12) will receive 2 cycles of AU-011 at the highest feasible and tolerated dose of 3 repeat 80 µg doses, each followed by 2 repeat laser applications. The second cycle of AU-011 will be administered no earlier than the Week 12 Visit and after resolution of any inflammation resulting from the first cycle or when the inflammation is minimal and decreasing based on investigator judgement. Cycle 2 should be administered as soon as reasonably possible after inflammation has resolved or is minimal and decreasing based on investigator judgement. However, if 2 subjects experience a DLT during treatment with Cycle 2, then no further subjects will receive Cycle 2 of AU-011 until discussed with the independent ocular oncologist and medical monitor and continuation of enrollment is confirmed. If the fovea is within 2 mm of the tumor edge or edge of the clinical margin of the tumor, an adjustment to the laser procedure should be performed on each treatment day of both cycles (as outlined in the Protocol section 8.2.2).

4.5.3 Laser Activation of AU-011

This study will use the Aura Photoactivation System which will deliver light at 689 nm to the CM 6 to 8 hours after the IVT administration (after the second IVT injection for the subjects receiving 80 µg doses) of study drug AU-011. A second laser application will also be investigated in this trial to ensure that maximum tumor cell necrosis occurs with each administration of Light-activated AU-011. The study procedures binder provides detailed instructions on the procedures for laser application for this study.

4.5.4 Treatment Cohorts

The treatment cohorts are defined as follow:

Dose Escalation cohorts:

- Cohort 1: 20 µg x 1 laser, Single
- Cohort 2: 40 µg x 1 laser, Single
- Cohort 3: 80 µg x 1 laser, Single
- Cohort 4: 40 µg x 1 laser, 2XQ. Wk
- Cohort 5: 40 µg x 1 laser, 3XQ. Wk
- Cohort 6: 80 µg x 2 lasers, Single
- Cohort 7: 80 µg x 1 laser, 3XQ. Wk
- Cohort 8: 80 µg x 2 lasers, 3XQ. Wk

Expansion cohorts:

- Cohort 9: 80 µg x 2 Lasers, 3XQ. Wk
- Cohort 10: Observational cohort - No documented growth
- Cohort 11: 2 Cycles of AU-011 – With or without documented growth
- Cohort 12: 2 Cycles of AU-011 – Documented growth

4.6 Calculated Variables

- Study day 1 is defined as the day when first study treatment was received.
- The baseline is defined as the last assessment done before or on study day 1. For instance, if data was collected at screening and Day 1, then the Day 1 value will be used for baseline
- Time since diagnosis of CM (months) = (month and year of screening – month and year of diagnosis).

Assessments done on the date of study treatment administration are assumed to take place before the administration, unless specified otherwise.

4.7 Partial Dates

Missing or incomplete dates will not be imputed at the data level. However, assumptions for missing or partial dates for important variables will be made to allow inclusion of appropriate data records in the analyses. In general, the assumptions about the missing or partial dates, when needed, are made conservatively to avoid overestimation of treatment effects and underestimation of adverse effects.

If a medication, procedure or surgery date is missing or partial, so it cannot be determined whether it was taken prior or concomitantly, it will be considered both as a prior and a concomitant medication, procedure or surgery.

If the partial AE onset date information does not indicate whether the AE started prior to treatment or after treatment, the AE will be classified as started after treatment.

4.8 Methods To Be Used For Handling Missing Data

When summarizing categorical variables, subjects with missing data are generally not included in the calculations of percentages unless otherwise specified. When needed, the category of "Missing" is created and the number of subjects with missing data is presented.

When summarizing continuous variables, subjects with missing data are not included in calculations. No imputations are made.

4.9 Changes to Analyses Specified in the Protocol

The tumor response categories criteria specified in Section 8.1 of this SAP are different than what is provided in the Sections 10.3.6 and 10.3.7 of the Protocol (Rev-15, 21 Feb. 2020). The tumor response categories and criteria provided in this SAP will be used.

5 Study Subjects

5.1 Disposition of Subjects

The number of subjects in each population will be tabulated by cohort (defined in Section 0), overall and subgroups (defined in Section 4.4).

The frequency of subjects treated, of subjects who completed the study treatment per protocol and of subjects who discontinued the study early will be given by cohort and overall for the ITT population. The primary reason for early discontinuation of study will be summarized. The details of the 'other reason' will be included in the listing.

5.2 Protocol Deviations

All protocol deviations will be assessed and identified by the sponsor. The major protocol deviations will be summarized for each cohort and overall for the ITT population. The details will be listed by subject and cohort. Listing of all in- and exclusion criteria not met will be provided by cohort separately.

6 Demographic and other Baseline Characteristics

Descriptive statistics with respect to demographics and subject characteristics at baseline will be displayed by cohort, overall, and subgroups (as needed, defined in Section 4.4) for the ITT population.

The variables to be summarized are:

- Age, gender, race, ethnicity
- Iris color, study eye,
- Tumor lesion thickness, tumor largest basal diameter, distance from the fovea, distance from the nerve, Risk factors
- History of Primary Choroidal Melanoma:
  - Eye affected (OS/OD/OU)
  - Time since diagnosis of CM (months)
  - Prior Treatment for CM (Yes/No)
- Vital signs: pulse, systolic and diastolic blood pressure (seated)
- Anti-drug antibody (ADA) sample
- Visual acuity score both in the study eye and in the fellow eye

- Ophthalmic history (other than primary CM) both in the study eye and in the fellow eye
- Medical history (other than ophthalmic history)

Medical and ophthalmic history will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 20.0 and will be tabulated by system organ class (SOC) and preferred term (PT) by cohort and overall for the ITT population. Multiple occurrences of the same preferred term in one subject will be counted only once. Summary tables will be sorted alphabetically by SOC then by PT within SOC based on descending frequency in the 'overall' column.

Other baseline data, for example, childbearing potential and contraception, serum pregnancy test, etc, will be provided in a data listing.

7 Prior and Concomitant Treatment

Prior and concomitant treatments will be summarised and listed for the ITT population.

7.1 Prior and Concomitant Medications

Prior and concomitant medications will be classified according to World Health Organization Drug Dictionary (Version 2017-March).

The number and percentage of subjects receiving a prior or concomitant medication will be displayed by first level Anatomical Therapeutic Chemical class (ATC 1) and fourth level Anatomical Therapeutic Chemical class (ATC 4) by cohort and overall for the safety population.

Medications will be reported as prior when they start before the first day of study treatment. Medications will be reported as concomitant when they start before, on or after first day of study treatment and continue afterwards. Medications started before the first day of study treatment and continuing afterwards will be reported both as prior and concomitant. In case of missing or partial start/stop date, rules defined in section 4.7 will be applied to identify prior and/or concomitant medications.

Prior and concomitant medication summaries will be sorted alphabetically by ATC 4 class within ATC 1 class.

A listing of all medications recorded on the prior and concomitant medications eCRF page will provide details including indication, start and stop dates and when available, dose, route, frequency.

7.2 Prior and Concomitant Procedures/Surgeries

Prior and concomitant procedures and surgeries will be coded using MedDRA version 20.0.

The number and percentage of subjects undergoing a prior or concomitant procedure or surgery will be displayed by system organ class and preferred term by cohort and overall for the safety population.

Procedures and surgeries will be reported as prior when they start before the first day of study treatment. Procedures and surgeries will be reported as concomitant when they start before, on or after first day of study treatment and continue afterwards. Procedures and surgeries started before the first day of study treatment and continuing afterwards will be reported both as prior and concomitant. In case of missing or partial date, rules defined in section 4.7 will be applied to identify prior and/or concomitant procedures and surgeries.

Prior and concomitant procedures and surgeries summaries will be sorted alphabetically by SOC then by PT within SOC based on descending frequency in the 'overall' column.

A listing of all procedures and surgeries recorded on the prior and concomitant procedures and surgeries eCRF page will provide details including indication, eye, and start and stop dates.

8 Efficacy Evaluation

Efficacy will be assessed at each visit for any potential tumor response based on imaging-based assessments, and changes in Early Treatment Diabetic Retinopathy Study (ETDRS) BCVA. No formal hypothesis testing will be performed in this study.

For imaging-based measurements, e.g. B-scan, OCTA, etc, as there are 2-3 readers and multiple values are available, and no adjudication will be conducted, a general convention will be followed: For the continuous variables, the average will be taken as the final value for analysis. For the categorical variables, if there are two like responses available, it will be the final response. And when all responses differ, the most conservative response will be taken as the final response.

Efficacy analyses will be performed by cohort, overall and for subgroups (defined in Section 4.4) on ITT population. Some efficacy analyses will also be performed on Efficacy Evaluable population as sensitivity analyses (see more details in Section 8.3).

8.1 Tumor Response

Three different methods of determining tumor response will be applied. The rationale for using these 3 methods is to describe the data taking into consideration various factors (ie, criteria as stated below) that could have impacted the determination of tumor response. The following four criteria will be considered for tumor response assessment:

a) The maximum thickness and LBD as defined in Section 8.1.1
b) The investigator determination of the subject meeting protocol defined disease progression criteria as defined in Section 8.1.2
c) The subject having an AE of Pigmentary Changes as defined in Section 8.1.3.
d) The subject receiving standard of care

The 3 different methods for determining tumor response are:

1. Based on maximum thickness and LBD and subject receiving Standard of Care

Tumor response (PR, SD, or DP) will be based on the algorithm as defined in Section 8.1.1, with the modification that Investigator determination mentioned in DP definition will not be considered and if a subject receives standard of care they will be considered as having met the disease progression (DP) criteria from the date standard of care was administered.

Note that for the Month 12 LOCF and Last Visit timepoints:

- If a patient receives standard of care prior to their Month 12 Visit, the subject will be considered as having met DP, even if the LBD and/or tumor thickness assessments are being LOCF'd from a time-point previous to the SOC being administered.
- Similarly, if a patient receives standard of care prior to their Last Visit, the subject will be considered as having met DP, even if the LBD and/or tumor thickness assessments are being LOCF'd from a time-point previous to the SOC being administered.

2. Based on maximum thickness and LBD, subject receiving Standard of Care, and Investigators determination of progression

Tumor response (PR, SD, or DP) will be based on the algorithm defined method 1 above with the addition of the Investigator determination of progression criteria provided in Section 8.1.2.

3. Based on maximum thickness and LBD, subject receiving Standard of Care, Investigators determination of progression, and adverse events of pigmentary changes

Tumor response (PR, SD, or DP) will be based on the algorithm defined method 1 with the additional criteria of both Investigator determination (Section 8.1.2) and AE of pigmentary changes provided in (Section 8.1.3).

As this method accounts for the Investigator determination of progression per protocol sections 10.3.4 and 10.3.7, it will be considered the primary method for describing the results in the clinical study report.

For each of these 3 methods of determining tumor response, the tumor response results will be presented at each visit, as well as an overall summary table. The overall summary table will present the results at Month 12 using last observation carried forward (LOCF) as well as the subject's last visit, including follow-up. For the overall summary table, the table will provide which of the LBD and maximum thickness criteria were met for the response (or both) as well as a category for "Treated with standard of care prior to Progression" (i.e., this category will be for subjects who were treated with standard of care prior to reaching the progression criteria).

An additional summary of the Summary of Tumor Response Tables (3 tables for Methods 1-3) including just site 009 (i.e., the site excluded from the Efficacy Evaluable Population) will be performed.

8.1.1 Maximum Thickness and LBD Tumor Response Criteria

All tumors will be assessed for thickness by B-scan ultrasound and for largest basal diameter (LBD) by Fundus Photos.

Criteria to classify tumor response will be:

- **Partial Response (PR)**:
  - Any reduction > 0.5 mm in the maximum thickness of the CM from baseline (B-scan) and no progression (ie, and increase <1.0 mm) based on LBD (Fundus Photos), **OR**
  - Any reduction > 0.5 mm in the LBD of the CM from baseline (Fundus Photos) and no progression (ie, and increase <0.5 mm) based on tumor thickness (B-scan)
- **Stable Disease (SD)**:
  - Maximum thickness of the CM is within -0.5 mm to +0.5 mm (inclusive) change from baseline (B-scan), **AND**
  - Maximum LBD of the CM is within -0.5 mm to +1.0 mm (inclusive) change in diameter from baseline (Fundus Photos)
- **Disease Progression:**
  - Any increase > 0.5 mm in the maximum thickness of the CM from baseline not judged by the Investigator to be due to inflammation/swelling or hemorrhage (B-scan), **OR**
  - Any increase > 1.0 mm in the LBD of the CM from baseline not judged by the Investigator to be due to inflammation/swelling, hemorrhage or pigmentary changes (Fundus Photos)

Missing LBD or maximum thickness values:

If both the LBD and maximum thickness values at a visit are missing, the tumor response will be set to missing for that visit.

If 1 of the 2 measurements is missing, the tumor response will be determined by just considering criteria as applied to the non-missing measurement. (note: this rule does not apply to the Month 12 LOCF and Last Visit endpoints where an LOCF algorithm for both tumor thickness and LBD will be applied, as described below).

Additionally, the following LOCF algorithm for tumor thickness and LBD will be applied for tumor response relative the Month 12 LOCF and Last Visit endpoints only (i.e., this LOCF algorithm does not apply to the individual visits, only the Month 12 LOCF and Last Visit timepoints).

- If a subject is missing a tumor thickness and/or their LBD assessments as a scheduled visit, an LOCF approach will be used to impute the missing data from the previous visits (ie, an LOCF approach will be applied to the tumor thickness and separately an LOCF approach will be applied to the LBD). If a patient has no non-missing post-baseline visits, the baseline value will be used. The assessment of tumor response (i.e., as described above) will be applied using the LOCF'd tumor thickness and LBD values.

8.1.2 Investigator Determination of Progression

The investigator determination of progression is based on the corresponding Investigator judgement of progression eCRF question:

> *Did the subject meet the protocol defined disease progression criteria and not yet receive additional therapy with standard of care (plaque brachytherapy, proton beam radiotherapy or enucleation) or additional therapy with AU-011 since the previous visit? (Yes/No Response).*

If the Response to this eCRF question is "No" and the subject met the criteria for disease progression (DP) based on the maximum thickness and LBD criteria defined in Section 8.1.1, then the tumor response will be classified as Stable Disease (SD).

Note that if a subject has started standard of care, they will be considered as having met the disease progression (DP) criteria from the date standard of care was administered.

Missing Investigator judgement of progression:

If the subject is missing the Investigator judgement of progression for a visit, the values from the subject's next non-missing Investigator judgement of progression will be used. If the subject does not have a next non-missing assessment (i.e., there are no subsequent assessments or they are all missing), the determination of the tumor response category will be based on the LBD and maximum thickness criteria values only (i.e., without consideration of the Investigator judgement of progression).

8.1.3 Adverse Events of Pigmentary Changes

For any disease progression (DP) tumor responses due to LBD defined in Method 1 (i.e., based on only meeting the LBD criterion, not based on meeting either the tumor thickness criterion or subject receiving Standard of Care), if the subject has an AE of pigmentary changes in the eye being assessed ***and*** the Investigator response to eCRF question is "No" per section 8.1.2 on or after the start date of this AE, then the tumor response will be classified as stable disease (SD).

An AE of pigmentary changes is any AE where the Preferred Term (PT) is "Retinal depigmentation" or "Retinal pigment epitheliopathy".

8.1.4 Subjects Receiving Standard of Care

The date of the subject receiving standard of care will be from the Prior and Concomitant Procedure/Surgery eCRF page. Standard of Care includes the eye procedures categorized as: 'Radiotherapy to eye', 'Brachytherapy to eye' or 'Photodynamic therapy' (i.e., dictionary derived terms).

8.1.5 Maximum Tumor Thickness by B-scan Ultrasound

Descriptive statistics for change from baseline in maximum tumor thickness as measured by B-scan ultrasound in the study eye will be summarized at each visit by cohort, overall and for subgroups (defined in Section 4.4).

8.1.6 Largest Basal Diameter by Fundus Photography

Descriptive statistics for change from baseline in largest tumor basal diameter as measured by color fundus photography in the study eye will be summarized at each visit by cohort, overall and for subgroups (defined in Section 4.4).

8.1.7 Tumor Reponse by B-scan Ultrasound and Largest Basal Diameter by Fundus Photography

Number and percentage of subjects with tumor control (PR and SD) on both tumor thickness and LBD and tumor progression on either tumor thickness or LBD in the study eye will be summarized at each visit by cohort, overall and for subgroups defined in Section 4.4. Definitions in Section 8.1 will be used.

8.1.8 Tumor thickness growth rate

Tumor thickness growth rates after treatment will be compared to historical growth rates in subjects with documented growth and other subgroups defined in section 4.4 using a mixed model repeated measures (MMRM) analysis. These analyses will be provided in a separate report by the sponsor.

8.2 Best Corrected Visual Acuity by ETDRS Protocol

The BCVA score or visual acuity score using the Early Treatment of Diabetic Retinopathy Study (ETDRS) protocol will be determined for each subject in each eye at each visit. The observed visual acuity score in the study eye will be used for the analyses.

Descriptive statistics for visual acuity score as well as for change from baseline in visual acuity score will be presented for each visit up to the Week 52 visit and at the end of study visit by cohort, overall and for subgroups (defined in Section 4.4).

Number and percentage of subjects with a 5, 10 or 15 letter gain or loss at each visit up to the Week 52 visit and at the end of study visit will also be included by cohort and overall. Number and percentage of subjects with visual acuity preservation (ie, not meeting visual acuity failure criteria as defined below) over 52 weeks will also be included overall and for subgroups (defined in Section 4.4).

Visual acuity failure is defined as having a ≥ 15 letter loss at Week 39 or Week 52 confirmed at the next visit excluding visits occurring post-SOC. Additional details are provided below:

- A ≥ 15 letter loss at Week 39 and confirmed at Week 52 (or at the next visit after Week 52 with non-missing data [regardless of the visit windowing algorithm as described in Section 4.1.2] if the subject's visual acuity data is missing at the Week 52 visit or the Week 52 visit did not occur). The data after a subject receives standard of care (SOC) is excluded (i.e., censored) from determination

of visual acuity failure. If there is no subsequent confirmatory visit data is available after Week 39 then the subject is counted as a visual acuity failure.

- If the subject does not meet the ≥ 15 letter loss criterion at Week 39 but does meet the ≥ 15 letter loss criterion at Week 52, then the subject's next visit after Week 52 with non-missing data (regardless of the visit windowing algorithm as described in Section 4.1.2) will be the confirmatory visit (i.e., the subject will be counted as a visual acuity failure if the subject's confirmatory visit also is a ≥ 15 letter loss). The data after a subject receives standard of care (SOC) is excluded (i.e., censored) from determination of visual acuity failure. If there is no subsequent confirmatory visit data is available after Week 52 then the subject is counted as failure.
- If SOC occurs before Week 39, the subject's 2 most recent visits available before SOC (with non-missing visual acuity data), regardless of the visit windowing algorithm as described in Section 4.1.2, will be used. If both visit assessments indicate the loss is ≥ 15 letters at this visit the subject will be counted as a visual acuity failure, otherwise the subject will not be counted as a visual acuity failure
- If both Week 39 and Week 52 visits are missing, the subject's 2 most recent visits before Week 39 (and before receiving SOC), regardless of the visit windowing algorithm as described in Section 4.1.2, with non-missing values will be used. If both visit assessments indicate the loss is ≥ 15 letters the subject will be counted as a visual acuity failure, otherwise the subject will not be counted as a visual acuity failure.
- If a subject does not have any post-treatment visual acuity data, the subject will not be counted as a visual acuity failure.

An additional summary of the following two tables including just site 009 (i.e., the site excluded from the Efficacy Evaluable Population) will be performed:

- Summary of Best Corrected Visual Acuity (ETDRS Letters) and Change from Baseline by Visit
- Number and percentage of subjects with visual acuity preservation (i.e., as defined above)

8.3 Sensitivity Analyses

The following sensitivity analyses will be performed:

- The maximum tumor thickness and largest basal diameter endpoints (i.e., as described in Sections 8.1.5 and 8.1.6, respectively) will be summarized on ITT population excluding post-standard of care data (i.e. all data after receiving standard of care will be excluded for the standard of care subjects).
- BCVA data (Section 8.2) will be summarized on ITT population excluding post-standard of care data. Number and percentage of subjects with a 5, 10 or 15 letter gain or loss at each visit up to the Week 52 visit and at the end of study visit will also be provided for: 1) Efficacy Evaluable population; 2) Efficacy Evaluable population excluding post-standard of care data.
- Tumor response (section 8.1.7) will be summarized on Efficacy Evaluable population.

8.4 Exploratory Analyses

Exploratory analyses will be performed for all other relevant parameters from EDI-OCT, color fundus photography, fluorescein angiography, and B-scan ultrasound.

Internal reflectivity of tumors by A-scan ultrasound and macular changes (foveal avascular zone and vessel density) by OCTA will be summarized at each visit as a sub-study for sites with A-scan diagnostic probes and OCTA devices.

These analyses will be performed on ITT population.

8.4.1 Subretinal Fluid by EDI-OCT

Shift tables presenting number and percentage of subjects with or without (presence/absence) subretinal fluid as measured by EDI-OCT in the study eye from baseline to each post-baseline visit will be produced by cohort and overall for the ITT population.

Descriptive statistics for change from baseline in central retinal thickness as measured by EDI-OCT in the study eye will be summarized for each visit by cohort and overall for the ITT population.

OCT is primary measurement for subretinal fluid.

8.4.2 Orange Pigmentation on Tumor by Color Fundus Photography

Shift tables presenting number and percentage of subjects with or without (presence/absence) orange pigmentation on tumor as measured by color fundus photography in the study eye from baseline to each post-baseline visit will be produced by cohort and overall for the ITT population.

Other fundus photography assessments data, i.e. Tumor Melanosis, Greatest Basal Area, Distance From Fovea, and Distance From Nerve Edge, will be summarized. And for categorical parameters, shift tables reflecting the changes from baseline will be produced at each visit by cohort and overall for the ITT population.

8.4.3 Other B-scan Ultrasound Data

Frequency distribution of Shape of Tumor (Dome, Collar button, Multi-lobe, Irregular, Flat, Other); Apical sub-retinal fluid (none, mild, moderate, significant); and Vitreous opacity (none, mild, moderate, dense, undetermined) will be tabulated for each visit by cohort and overall for the ITT population.

8.4.4 Capillary Density by OCTA

Descriptive statistics of foveal avascular zone area, and vessel density in the study eye for the actual values and change from baseline values will be summarized for baseline, at week 26, 52 and week 104 visits by cohort and overall for the ITT population.

9 Safety Evaluation

Safety analyses will be performed by cohort and overall for the safety population.

The main safety analyses will be based on all available data regardless of additional therapy.

9.1 Extent of Exposure

Number and percentage of subjects administered with AU-011, who received full dose of AU-011 (Yes/No), Light activated (Yes/No), administered with first laser treatment (Yes/No, if applicable), administered with second laser treatment (Yes/No, if applicable), will be summarized at Day 1, Day 8 and Day 15 visits.

Details of the treatment administration for each individual subject will be provided in a data listing.

9.2 Dose Limiting Toxicities

Dose limiting toxicity[ies] (DLT[s]) is defined as a drug-related safety event, severe enough to limit dose escalation (increase of dose or frequency of dosing) of AU-011.

Number and percentage of subjects with DLTs will be tabulated by cohort and overall for the safety population.

9.3 Adverse Events

Adverse events (AEs) will be coded using the MedDRA Version 20.0 and will be graded according to the National Center Institute Common Terminology Criteria for AEs (NCI-CTCAE criteria [v4.03]). Uncoded terms will be presented under "SOC uncoded", with their reported term.

Related AEs are defined as events with a relationship to study treatment equal to 'related' or with missing relationship. All AEs related to study drug, related to injection procedure, and related to laser administration will be reported separately.

Adverse events in this section will be tabulated if they are treatment-emergent (TE). Non-TE adverse events will only be included in listing of all adverse events. Adverse events which begin on or after the day the treatment is initiated will be considered as treatment-emergent adverse events (TEAEs). Missing or partial AE start date will be estimated in order to include events in summary tables in case of doubt (see section 4.7 for more details).

Ocular TEAEs are those TEAEs reported as occurring in the eye(s).

All tabulations of adverse events will be presented by cohort, overall, and subgroups (defined in Section 4.4).

An overall summary table of AEs will present the number and percentage of subjects with at least one:

- TEAE
- Serious AE (SAE)
- Related SAE – broken out by study drug, injection procedure and laser related
- Ocular TEAE in the study eye
- Related ocular TEAE in the study eye – broken out by study drug, injection procedure and laser related
- Ocular TEAE in the fellow eye
- Related ocular TEAE in the fellow eye – broken out by study drug, injection procedure and laser related
- Non-ocular TEAE
- Related non-ocular TEAE – broken out by study drug, injection procedure and laser related
- Fatal AE

Tabulations of the number of subjects who experienced TEAEs as well as number of events will be presented by system organ class and preferred term (in descending frequency by SOC and by PT within each SOC). Subjects will only be counted once for each preferred term. In case a subject experienced the same event more than once, the event will be counted only once.

The following tabulations will be presented:

- All TEAEs
- Ocular TEAEs in the study eye
- Related ocular TEAEs in the study eye – broken out by study drug, injection procedure and laser related. Three additional tabulations include:
    - Related to study drug and/or injection procedure and/or laser
    - Related to study drug and/or laser
    - Related to injection procedure that are not related to study drug or laser
- Ocular TEAEs in the fellow eye
- Related ocular TEAEs in the fellow eye – broken out by study drug, injection procedure and laser related, if relevant
- Non-ocular TEAEs
- Related non-ocular TEAEs – broken out by study drug, injection procedure and laser related

In addition, tabulations of the number of subjects who experienced TEAEs as well as number of events will be presented by system organ class, preferred term and worst severity. Subjects will only be counted once for each preferred term. In case a subject experienced the same event more than once, the event with the worst severity will be counted in the summary.

The following tabulations will be presented:

- All TEAEs
- Ocular TEAEs in the study eye
- Related ocular TEAEs in the study eye – broken out by study drug, injection procedure and laser related. Three additional tabulations include:
    - Related to study drug and/or injection procedure and/or laser
    - Related to study drug and/or laser
    - Related to injection procedure that are not related to study drug or laser
- Related non-ocular TEAEs – broken out by study drug, injection procedure and laser related

Listing of all adverse events by cohort will be provided including the subject identifier, age, race, sex, reported term, preferred term, start date (Study Day of Start), stop date (Study Day of Stop), duration, TEAE (Yes/No), DLT (Yes/No), serious (Yes/No), associated eye (OD/OS/OU), severity (Mild/Moderate/Severe/Life-Threatening/Death), relationships (Related/Not Related to each of study drug, injection procedure, and laser administration), outcome, action taken. The adverse event listing will be sorted by treatment arm, subject identifier, start date, and reported term.

9.4 Deaths and Serious Adverse Events

SAEs, related SAEs and fatal AEs will be summarized by system organ class and preferred term. In addition, listings of SAEs and fatal AEs will be provided, similarly to the listing of all AEs.

9.5 Clinical Laboratory Determination

Clinical laboratory parameters will be graded (as applicable) using the NCI-CTC version 4.03. Laboratory parameters which cannot be graded will be given the designation of

'Normal' or 'Abnormal', where 'Abnormal' is defined as outside of the normal range of [LLN, ULN]. Parameters to be summarized are as follows:

- **Hematology and Differential Panel:** Hemoglobin, hematocrit, Red Blood Cells (RBC), White Blood Cells (WBC), WBC differential, platelets, Mean Corpuscular Volume (MCV).
- **Biochemistry and electrolytes:** Total bilirubin, direct bilirubin, alkaline phosphatase, ALT (SGPT), AST (SGOT), GGT, LDH, blood urea nitrogen (BUN), creatinine, glucose, uric acid, calcium, phosphorus (or phosphate), total protein, albumin, globulin, triglycerides, cholesterol, CK, sodium, potassium, bicarbonate, chloride, and magnesium

For continuous laboratory parameters, summaries of the values and changes from baseline will be presented for each visit by parameter.

Where applicable, the shift from baseline NCI-CTC grade to worst post-baseline NCI-CTC grade will be presented for each parameter. This summary will include all scheduled and unscheduled post-baseline visits in the derivation of worst post-baseline grade.

For parameters without NCI-CTC grading, the shift from baseline abnormality categorization ('Normal', 'Abnormal') to worst post-baseline abnormality categorization ('Normal', 'Abnormal') will be presented for each parameter. This summary will include all scheduled and unscheduled post-baseline visits in the derivation of the worst post-baseline abnormality categorization.

9.6 Vital Signs, Physical Findings and Other Observations Related to Safety

9.6.1 Vital Signs

Descriptive statistics for the actual values and change from baseline values of the vital signs parameters will be summarized at each visit by cohort and overall for the safety population. The vital sign parameters to be summarized are Systolic Blood Pressure (mmHg), Diastolic Blood Pressure (mmHg) and Pulse Rate (beats/min).

9.6.2 Slit Lamp Biomicroscopy

Number and percentage of subjects with normal/abnormal slit lamp biomicroscopy exam in the study eye will be summarized for Motility, Lids/Lacrimal/Lashes, Conjunctiva/Sclera, Cornea, Iris, Pupils, Optic Nerve and Retina parameters at each visit by cohort and overall for the safety population.

Number and percentage of subjects with anterior chamber activity (cells: 0, Trace, 1+, 2+, 3+, 4+) in the study eye will be summarized at each visit by cohort and overall for the safety population.

Number and percentage of subjects with lens status aphakic/pseudo-phakic/phakic as well as complete grade nuclear, posterior subcapsular cataract (PSC) and cortical (0, 1, 2, 3, 4), if phakic, and vitreous haze (0, 1+, 2+, 3+, 4+) in the study eye will be summarized at each visit by cohort and overall for the safety population.

The shift from baseline to week 12, week 52 and week 104 visits for each parameter in the study eye will be presented by cohort and overall for the safety population.

9.6.3 Visual Field Exam

Results of automated perimetry exam in the study eye and the fellow eye will be provided in a data listing for the safety population.

9.6.4 Tonometry

Descriptive statistics of the IOP in the study eye for the actual values and change from baseline values will be summarized at each visit by cohort and overall for the safety population. In case of multiple post-baseline values, only the first value will be taken into account at each visit. All values will be included in the data listing.

9.6.5 Fundoscopy

Number and percentage of subjects with normal/abnormal fundoscopy exam in the study eye will be summarized for each visit by cohort and overall for the safety population. The shift from baseline to week 12, week 52 and week 104 visits for fundoscopy exam in the study eye will be presented by cohort and overall for the safety population.

9.6.6 Anti-Drug Antibodies

Number and percentage of subjects with positive/negative ADA test result will be summarized at each timepoint by cohort and overall for the safety population.

9.6.7 Additional Therapy

Some subjects may receive additional therapies with AU-011 or standard care after Visit 11 (Week 12) if the Investigator determines that ocular melanoma has progressed and further treatment (additional therapy) is required. Number and percentage of those subjects who receive AU-011 will be summarized by original cohorts and overall. The highest established safe dose and regimen of drug and laser that was given at the time of the request will also be present.

Number and percentage of subjects receiving additional therapy other than AU-011 will be summarized by cohort and overall for the safety population. Details of the treatment administration for each individual subject will be provided in a data listing.

10 Interim Analysis

Two interim analyses were planned to summarize the safety and efficacy results of AU-011 as mentioned in Section 4.2.

One interim analysis was performed for the '01AUG2018 Deliverable". It has been decided that no additional interim analysis will be performed.

11 Appendices

11.1 Schedule of Assessments

	Screening	Active Period						Follow-up Period								End of Study or Early Termination
Assessment	**Visit 1 D -28 to 1**	**Visit 2 D1**	**Visit 3 D2 ± 4H**	**Visit 4 D8 + 1D**	**Visit 5 D9 ± 4H**	**Visit 6 [o] D15 + 1D**	**Visit 7 D16 ± 4H**	**Visit 8 D29± 1D**	**Visit 9 W6 ± 3D**	**Visit 10 W8 ± 3D**	**Visit 11 W12 ± 3D**	**Visit 12 W26 ± 7D**	**Visit 13 W39 ± 7D**	**Visit 14 W52 ± 7D**	**Visit 15 W78 ± 7D**	**Visit 16 W104 ± 7D or Early Termination**
Informed consent	X															
Eligibility review	X	X														
Demographics	X															
Medical and ophthalmic history	X															
Vital signs[a]	X	X	X	X	X[j]	X	X[k]	X						X		X
Pregnancy test	X	X[b]														
Laboratory assessments (CBC with differential and CMP)	X[c]	X[c]		X[c]				X[c]								
Light-activated AU-011 treatment		X[d]		X[j]		X[k]										
ADA samples	X			X		X[k]		X			X			X		
BCVA	X	X[e]	X	X	X[j]	X	X[k]	X	X	X	X	X	X	X	X	X
Slit lamp biomicroscopy[f]	X	X	X	X	X[j]	X	X[k]	X	X	X	X	X	X	X	X	X
IOP[f]	X	X	X	X	X[j]	X	X[k]	X	X	X	X	X	X	X	X	X
Fundoscopy[f]	X	X	X	X	X[j]	X	X[k]	X	X	X	X	X	X	X	X	X
Fundus photos[f]	X	X[e]	X	X	X[j]	X	X[k]	X	X	X	X	X	X	X	X	X
FA[f]	X										X			X		X
EDI-OCT[f]	X	X[e]	X	X	X[j]	X	X[k]	X	X	X	X	X	X	X	X	X
OCTA[f, p]	X	X[e]	X	X	X[j]	X	X[k]	X	X	X	X	X	X	X	X	X
B-scan[f]	X	X[e]	X[l]	X		X		X		X	X	X	X	X	X	X
A-scan (study eye only)	X			X				X		X	X	X	X	X	X	X
Visual field exam[f]	X										X			X		X
AE review[q]	X[q]	X	X	X	X[j]	X	X[k]	X	X[m]	X[n]	X[h,q]	X[h,q]	X[h,q]	X[h,q]	X[h,q]	X[h,i,q]
Concomitant medication review[q]	X	X	X	X	X[j]	X	X[k]	X	X[j]	X[k]	X[q]	X[q]	X[q]	X[q]	X[q]	X[g,q]

[a]Vital signs include BP seated and pulse.
[b]Serum pregnancy test will be performed at Visit 1. If Visit 2 occurs more than 7 days after Visit 1, then urine pregnancy test will be performed at Visit 2.
[c]CBC with differential includes hemoglobin, hematocrit, red blood cells (RBC), white blood cells (WBC), WBC differential, and platelets. CMP includes total bilirubin, direct bilirubin, alkaline phosphatase, ALT (SGPT), AST (SGOT), GGT, LDH, blood urea nitrogen (BUN), creatinine, glucose, uric acid, calcium, phosphorus (or phosphate), total protein, albumin, globulin, triglycerides, cholesterol, CK, sodium, potassium, bicarbonate, chloride, and magnesium. If Visit 2 occurs more than 7 days after Visit 1, then laboratory assessments will be repeated at Visit 2.
[d]Subjects should remain at the study site following intravitreal injection until approximately ½ hour after laser treatment. If subjects are discharged during daylight hours, appropriate sun protection, e.g., sunglasses and a hat, will be required.
[e]If Visit 1 and Visit 2 are within 7 days, the following procedures do not need to be repeated prior to AU-011 study drug injection, unless clinically indicated: BCVA, fundus photos, EDI-OCT, OCTA, and B-scan.
[f]FA and Fundus photos, EDI-OCT, OCTA, B-scan, Visual Field, IOP, Slit lamp and Fundoscopy will be performed in both eyes at Visit 1 (Screening) and Visit 11 (Week 12), and at any Early Termination Visit if that occurs before Visit 11 (Week 12), and in the study eye only at all remaining visits where applicable for each assessment.
[g]If Early Termination Visit occurs ≤ 30 days following study treatment.
[h]Study product and/or study procedure related AEs only for Cohorts 1 to 9.
[i]Any AE for up to 30 days after the last AU-011 treatment if Early Termination Visit occurs ≤ 30 days following study treatment.
[j]For 2 and 3 Repeat Light-activated AU-011 administration cohort subjects only
[k]For 3 Repeat Light-activated AU-011 administration cohort subjects only
[l]For Cohort 1, 2 and 3 subjects only
[m]For Single Light-activated AU-011 administration cohort subjects, only study product and/or study procedure related AEs. For 2 and 3 Repeat Light-activated AU-011 administration cohort subjects, any AE.
[n]For Single Light-activated AU-011 administration cohort and 2 Repeat Light-activated AU-011 administration cohort subjects, only study product and/or study procedure related AEs. For 3 Repeat Light-activated AU-011 administration cohort subjects, any AE.
[o]For the observation cohort (Cohort 10) every 3 month visits (i.e. 90 day (+/- 7 days) intervals from the Screening Visit) prior to evidence of tumor growth, all procedures outlined for Visit 6 (Day 15) will be performed with the exception of OCTA and Anti-drug Antibody (ADA) testing which is not required.
[p]For Cohort 6, 7, 8, and 9 subjects only
[q]For Cohort 10, 11, and 12 subjects, all SAEs and AEs and concomitant medications will be reported from the time the subject signs the informed consent through their last study visit.

11.2 Definition of Visit Windows in Reporting

The definition of visit label and visit windows in reporting are described in the table below.

Study Period	Visit Label	Definition [Day window]
Screening	Visit 1	= Subject screening date; nominally 1 to 28 days prior to the first AU-011 treatment. 'Day 1' - 'Date of assessment' = [1 to 28]. Alternatively, this is the assessment before the first treatment date.
Active Period	Visit 2 - D1 (Baseline)	= An assessment with the same date as recorded on the Day 1 Administration CRF Target date = 1
	Visit 3 – D2	= An assessment where 'Date of assessment' – 'Day 1' + 1 = 2 Target date = 2
	Visit 4 – D8	= An assessment where 'Date of assessment' – 'Day 1' + 1 = [8 - 9] Target date = 8
	Visit 5 – D9	= An assessment where 'Date of assessment' – 'Day 1' + 1 = [9 - 10] Target date = 9. Alternatively, this is the assessment one day after Visit 4 – D8.
	Visit 6 - D15	= An assessment where 'Date of assessment' – 'Day 1' + 1 = [15 - 16] Target date = 15
	Visit 7 - D16	= An assessment where 'Date of assessment' – 'Day 1' + 1 = [15 - 17] Target date = 16. Alternatively, this is the assessment one day after Visit 6 – D15.
Follow-up Period	Visit 8 – D29	= An assessment where 'Date of assessment' – 'Day 1' + 1 = [22 - 36] Target date = 29
	Visit 9 – W6	= An assessment where 'Date of assessment' – 'Day 1' + 1 = [37 - 50] Target date = 43
	Visit 10 – W8	= An assessment where 'Date of assessment' – 'Day 1' + 1 = [51 - 64] Target date = 57
	Visit 11 – W12	= An assessment where 'Date of assessment' – 'Day 1' + 1 = [65 - 113] Target date = 85
	Visit 12 – W26	= An assessment where 'Date of assessment' – 'Day 1' + 1 = [155 - 211] Target date = 183
	Visit 13 – W39	= An assessment where 'Date of assessment' – 'Day 1' + 1 = [246 - 302] Target date = 274
	Visit 14 – W52	= An assessment where 'Date of assessment' – 'Day 1' + 1 = [337 - 393] Target date = 365
	Visit 15 – W78	= An assessment where 'Date of assessment' – 'Day 1' + 1 = [463 - 631] Target date = 547
End of Study	Visit 16 – W104	= An assessment where 'Date of assessment' – 'Day 1' + 1 = [700 - 756] Target date = 728

11.3 List of Tables/Graphs/Listings

11.3.1 List of Statistical Tables

Table Number	Title
14.1.1.1	Study populations – All Screened Subjects
14.1.1.2	Subject Disposition – ITT Population
14.1.1.3	Summary of Major Protocol Deviations – ITT Population
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14.1.2.2	Baseline Tumor Characteristics – ITT Population
14.1.2.3	Baseline Visual Acuity Score (ETDRS Letters) – ITT Population
14.1.3.1	History of Primary Choroidal Melanoma – ITT Population
14.1.3.2	Ophthalmic History (Other Than Primary CM) by System Organ Class and Preferred Term – Study Eye – ITT Population
14.1.3.3	Ophthalmic History (Other Than Primary CM) by System Organ Class and Preferred Term – Fellow Eye – ITT Population
14.1.3.4	Medical History (Excluding Ophthalmic History) by System Organ Class and Preferred Term – ITT Population
14.1.4.1	Prior Medications by ATC Code 1 and ATC Code 4 – ITT Population
14.1.4.2	Concomitant Medications by ATC Code 1 and ATC Code 4 – ITT Population
14.1.4.3	Prior Procedures/Surgeries by System Organ Class and Preferred Term – ITT Population
14.1.4.4	Concomitant Procedures/Surgeries by System Organ Class and Preferred Term – ITT Population
14.2.1.1	Summary of Maximum Tumor Height (B-scan) and Change from Baseline in by Visit - Study Eye – ITT Population
14.2.1.2	Summary of Largest Basal Diameter (Fundus Photography) and Change from Baseline by Visit - Study Eye – ITT Population
14.2.1.3.1	Summary Of Tumor Response (Method 1) – Study Eye - ITT Population
14.2.1.3.2	Summary Of Tumor Response (Method 2) – Study Eye - ITT Population
14.2.1.3.3	Summary Of Tumor Response (Method 3) – Study Eye - ITT Population
14.2.1.3.4	Summary Of Overall Tumor Response (Method 1) – Study Eye - ITT Population
14.2.1.3.5	Summary Of Overall Tumor Response (Method 2) – Study Eye - ITT Population
14.2.1.3.6	Summary Of Overall Tumor Response (Method 3) – Study Eye - ITT Population
14.2.1.3.7	Summary Of Overall Tumor Response (Method 1) – Study Eye - ITT Population (Site 009 only)
14.2.1.3.8	Summary Of Overall Tumor Response (Method 2) – Study Eye - ITT Population (Site 009 only)
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14.2.2.1	Summary of Visual Acuity Score (ETDRS Letters) and Change from Baseline by Visit – Study Eye - ITT Population
14.2.2.2	Proportion of Subjects with 5, 10, 15 Letters Gain/Loss of Vision by Visit – Study Eye - ITT Population
14.2.2.3	Number and Percentage of Subjects with Visual Acuity Preservation – Study Eye - ITT Population
14.2.2.4	Summary of Visual Acuity Score (ETDRS Letters) and Change from Baseline by Visit – Study Eye - ITT Population (Site 009 only)
14.2.2.5	Number and Percentage of Subjects with Visual Acuity Preservation – Study Eye - ITT Population (Site 009 only)
14.2.3.1.1	Sensitivity Analysis - Summary of Maximum Tumor Height (B-scan) and Change from Baseline in by Visit - Study Eye – ITT Population *excluding all Post-standard of care data*
14.2.3.1.2	Sensitivity Analysis - Summary of Largest Basal Diameter (Fundus Photography) and Change from Baseline by Visit - Study Eye – ITT Population *excluding all Post-standard of care data*

14.2.3.2.1	Sensitivity Analysis - Summary of Visual Acuity Score (ETDRS Letters) and Change from Baseline by Visit – Study Eye - ITT Population *excluding all Post-standard of care data*
14.2.3.2.2	Sensitivity Analysis - Proportion of Subjects with 5, 10, 15 Letters Gain/Loss of Vision by Visit – Study Eye - ITT Population *excluding all Post-standard of care data*
14.2.3.2.3	Sensitivity Analysis - Proportion of Subjects with 5, 10, 15 Letters Gain/Loss of Vision by Visit – Study Eye – Efficacy Evaluable Population
14.2.3.2.4	Sensitivity Analysis - Proportion of Subjects with 5, 10, 15 Letters Gain/Loss of Vision by Visit – Study Eye – Efficacy Evaluable Population *excluding all Post-standard of care data*
14.2.3.3.1	Sensitivity Analysis - Summary Of Tumor Response (Method 1) – Study Eye - EFFICACY EVALUABLE Population
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14.2.3.3.3	Sensitivity Analysis - Summary Of Tumor Response (Method 3) – Study Eye - EFFICACY EVALUABLE Population
14.2.3.3.4	Sensitivity Analysis - Summary Of Overall Tumor Response (Method 1) – Study Eye - EFFICACY EVALUABLE Population
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14.2.5.5	Summary Of Distance From Nerve Edge By Fundus Photography – Study Eye – ITT Population
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14.2.6.2	Summary of Apical Sub-retinal Fluid by B-Scan – Study Eye – ITT Population
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14.2.6.5	Summary Of Foveal Avascular Zone Area by Octa - Study Eye – ITT Population
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14.3.1.1	Extent of Exposure – AU-011 and Laser – SAF Population
14.3.1.2	Summary Of Additional Treatment – SAF Population
14.3.1.3	Summary of Dose Limiting Toxicities – SAF Population
14.3.2.1	Overview of Treatment-emergent Adverse Events (TEAE) – SAF Population
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14.3.2.3.1	Ocular Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Study Eye – SAF Population
14.3.2.3.2-7	Related Ocular Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Study Eye – SAF Population
14.3.2.4.1	Ocular Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Fellow Eye – SAF Population
14.3.2.4.2-4	Related Ocular Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Fellow Eye – SAF Population

14.3.2.5.1	Non-Ocular Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – SAF Population
14.3.2.5.2-4	Related Non-Ocular Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – SAF Population
14.3.2.6.1	Treatment-Emergent Adverse Events by Worst Severity, by System Organ Class and Preferred Term– SAF Population
14.3.2.6.2	Ocular Treatment-Emergent Adverse Events by Worst Severity, by System Organ Class and Preferred Term – Study Eye – SAF Population
14.3.2.6.3-8	Related Ocular Treatment-Emergent Adverse Events by Worst Severity, by System Organ Class and Preferred Term – Study Eye – SAF Population
14.3.2.7.1-3	Related Non-Ocular Treatment-Emergent Adverse Events by Worst Severity, by System Organ Class and Preferred Term – SAF Population
14.3.3.1	Serious Adverse Events by System Organ Class and Preferred Term – SAF Population
14.3.3.2-4	Related Serious Adverse Events by System Organ Class and Preferred Term – SAF Population
14.3.3.5	Adverse Events Leading to Death by System Organ Class and Preferred Term – SAF Population
14.3.4.1	Hematology: Values and Changes from Baseline by Visit – SAF Population
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14.3.4.4	Biochemistry – Shift From Baseline NCI-CTC Grade To Worst Post-Baseline NCI-CTC Grade
14.3.5.1	Vital Signs - Values and Change from Baseline by Visit – SAF Population
14.3.5.2	Summary of Intraocular Pressure (IOP) at each Visit – Study Eye - Safety Population
14.3.5.3	Summary of Intraocular Pressure (IOP) Increase on Treatment Days – Study Eye - Safety Population
14.3.6.1.1-8	Slit Lamp Biomicroscopy Exam: Descriptive Statistics (Frequencies) by Visit – Study Eye – SAF Population *--- For Parameters: Motility, Lids/Lacrimal/Lashes, Conjunctiva/Sclera, Cornea, Iris, Pupils, Optic Nerve and Retina*
14.3.6.2.1-4	Slit Lamp Biomicroscopy Exam: Descriptive Statistics (Frequencies) by Visit – Study Eye – SAF Population *--- For Parameters: Anterior Chamber Activity , Vitreous Haze, Lens Status, Lens Status - Phakic*
14.3.6.3.1-8	Slit Lamp Biomicroscopy Exam: Shift from Baseline to Week 12, 52 and 104 – Study Eye – SAF Population *--- For Parameters: Motility, Lids/Lacrimal/Lashes, Conjunctiva/Sclera, Cornea, Iris, Pupils, Optic Nerve and Retina*
14.3.6.4.1-3	Slit Lamp Biomicroscopy Exam: Shift from Baseline to Week 12, 52 and 104 – Study Eye – SAF Population *--- For Parameters: Anterior Chamber Activity , Vitreous Haze, Lens Status*
14.3.7.1	Fundoscopy Exam: Descriptive Statistics (Frequencies) by Visit – Study Eye – SAF Population
14.3.7.2	Fundoscopy Exam: Shift from Baseline to Week 12, 52 and 104 – Study Eye – SAF Population
14.3.7.3	Anti-Drug Antibodies: Descriptive Statistics (Frequencies) by Timepoint – SAF Population

11.3.2 List of Graphs

Graph Number	Title
14.2.1.1	Mean Change in Maximum Tumor Thickness from Baseline as Measured by B-scan Ultrasound – ITT Population
14.2.1.2	Mean Change in Largest Tumor Basal Diameter as Measured by Fundus Photography – ITT Population
14.2.1.3	Mean Change in Visual Acuity (in ETDRS Letters) Over Time – ITT Population
14.2.2.1	Sensitivity Analysis - Mean Change in Maximum Tumor Thickness from Baseline as Measured by B-scan Ultrasound – ITT Population *excluding all Post-standard of care data*
14.2.2.2	Sensitivity Analysis - Mean Change in Largest Tumor Basal Diameter as Measured by Fundus Photography – ITT Population *excluding all Post-standard of care data*
14.2.2.3	Sensitivity Analysis - Mean Change in Visual Acuity (in ETDRS Letters) Over Time – ITT Population *excluding all Post-standard of care data*

11.3.3 List of Derived Data Listings

Listing Number	Title
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16.1.2.2	Listing of Inclusion and Exclusion Criteria Not Met – ITT Population
16.1.3	Listing of Demographics and other Baseline Characteristics – ITT Population
16.1.4.1	Listing of Ophthalmic History – ITT Population
16.1.4.2	Listing of Other Medical History – ITT Population
16.1.5	Listing of Baseline Ophthalmic Examinations Information – ITT Population
16.1.6.1	Listing of Prior and Concomitant Medications – ITT Population
16.1.6.2	Listing of Prior and Concomitant Procedures/Surgeries – ITT Population
16.2.1	Listing of B-scan Parameters – Study Eye – ITT Population
16.2.2	Listing of Fundus Photos Parameters – Study Eye – ITT Population
16.2.3	Listing of BCVA Parameters – Study Eye – ITT Population
16.2.4	Listing of EDI-OCT Parameters – Study Eye – ITT Population
16.2.5	Listing of FA Parameters – Study Eye – ITT Population
16.2.6	Listing of A-scan Parameters – Study Eye – ITT Population
16.2.7	Listing of OCTA Parameters – Study Eye – ITT Population
16.3.1	Listing of Exposure to AU-011 and Laser – SAF Population
16.3.2	Listing of Dose Limiting Toxicities – SAF Population
16.3.3.1	Listing of Adverse Events – SAF Population
16.3.3.2	Listing of Serious Adverse Events – SAF Population
16.3.3.3	Listing of Fatal Adverse Events – SAF Population
16.3.4	Listing of Laboratory Data –SAF Population
16.3.5	Listing of Vital Signs – SAF Population
16.3.6	Listing of Slit Lamp Biomicroscopy Results – Study Eye – SAF Population
16.3.7	Listing of Tonometry Results – Study Eye – SAF Population
16.3.8	Listing of Fundoscopy Results – Study Eye – SAF Population
16.3.9	Listing of Visual Field Exam – Study Eye – SAF Population
16.3.10	Listing of Anti-Drug Antibodies – SAF Population
16.3.11	Listing of Additional Therapies – SAF Population