NCT05202808

# PROTOCOL CSP-029

## RXSIGHT LIGHT ADJUSTABLE LENS (LAL) AND LIGHT DELIVERY DEVICE (LDD) NEW ENROLLMENT STUDY

**RxSight, Inc.**
**100 Columbia, Suite 120**
**Aliso Viejo, CA 92656**

**Version 09**
**January 20, 2023**

I have read and agree to follow the procedures as outlined in this protocol.

This protocol contains confidential proprietary information with respect to RxSight products and clinical trials. I agree to hold this information in confidence and not to disclose it to any third parties for a period of five years from the date of this agreement, or until this information becomes a matter of public knowledge through no action or failure on my part to maintain its confidentiality.

_____
Site Name

_____ _____
*Principal Investigator's Signature* *Date*

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# RXSIGHT, INC.

# PROTOCOL NO. CSP-029

# RXSIGHT LIGHT ADJUSTABLE LENS (LAL) AND LIGHT DELIVERY DEVICE (LDD) NEW ENROLLMENT STUDY

## 1 STUDY SYNOPSIS

### STUDY DESIGN

This is a two phased study that will include Phase A (complete) and Phase B.

Phase A

The primary objective of Phase A was to develop a patient-reported outcome (PRO) instrument that assessed erythropsia after LDD light treatments, the "Daily Life Erythropsia Questionnaire" (DLEQ). This was a non-interventional, cross-sectional study at 1-3 sites with primary data collection from patients who had undergone cataract surgery with implantation of the RxSight LAL and had treatment performed with the Light Delivery Device. Phase A was designed to use approximately [redacted] English speaking patients at sites in the European Union where the device has a CE Mark.

Qualitative research interviews were conducted with adult patients who reported experiencing erythropsia to their eye care provider after treatment with the Light Delivery Device. These patients were identified, invited to participate, and interviewed within 8 weeks of a report of the erythropsia symptom. Cognitive debriefing methods were used during the interviews: (1) to ensure the questionnaire captures relevant aspects of erythropsia from the patient perspective, (2) to evaluate the clarity of each question, and (3) to assess response options for each question to ensure options capture the range of patient experiences (e.g., frequency, light conditions). Cognitive interviews and qualitative coding were to be conducted in up to three rounds of interviews and analysis with about eight patients per round. This allowed an iterative approach to the cognitive interviews and instrument modification: the DLEQ was tested with patients in the first round of interviews; following participant feedback modifications were made to the DLEQ; the revision was tested in the second round of patient interviews; based on participant feedback adjustments were made to the instrument. An optional third and final round of interviews was determined not to be needed as further changes were not required. The instrument was revised to incorporate patients' words to support its content validity and to increase the clarity and understandability of items that will be used to assess patient experiences with erythropsia.

There were no assessments of treatment effectiveness or safety associated with this phase for PRO development. There were no laboratory assessments associated with this research. This protocol was submitted to an Institutional Review Board(s)/Ethics Committee as required for studies with primary data collection from patients.

Patients treated in a commercial setting were evaluated using the following inclusion/exclusion criteria.

INCLUSION CRITERIA

- Adult patients (40 to 80 years of age) that had implantation of the RxSight Light Adjustable Lens (LAL™).
- Patient reported experiencing erythropsia to their eye care provider after treatment with the Light Delivery Device within the past eight weeks.
- Patient is able to read, write, speak, and understand English.
- Patient is willing and able to comprehend and sign a written informed consent prior to study entry.

EXCLUSION CRITERIA

- Patient has a clinically-relevant medical or psychiatric condition which, in the opinion of the investigator and/or coordinator, would interfere with completing the study including, but not limited to, sensory problems, cognitive impairment, acute mental illness or inadequately treated depression or anxiety.
- Complications during cataract surgery that would complicate evaluation of the erythropsia symptom.

Phase B

Phase B is a prospective, randomized, controlled, multicenter, post approval study of the RxSight LAL and LDD to be conducted at up to 15 clinical sites. It will begin after development of the "Daily Life Erythropsia Questionnaire" PRO is complete and has been accepted by FDA. This is a new enrollment study that is expected to last up to 30 months and include up to 12 study visits. Subjects will be randomized in a 2:1 ratio to receive either the RxSight LAL or a monofocal IOL (Control).

Patients who require cataract extraction and intraocular lens implantation will be screened for eligibility. If it is determined that the patient may be eligible to participate, study staff will explain the study purpose, procedures, risks/benefits and subject responsibilities to the potential participant. Written informed consent will be obtained prior to any study specific testing. The patient is enrolled upon signing the informed consent.

Subjects with preoperative corneal astigmatism of ≥0.75 D, without pre-existing macular disease, and meeting all inclusion/exclusion criteria will be randomly assigned in a 2:1 ratio to receive either the RxSight LAL or a commercially available monofocal IOL (Control).

Commencing at the Postop Week 3 visit, eyes will be refracted and undergo visual testing. Eyes implanted with the RxSight LAL will receive a power adjustment based on the manifest refraction. Eyes measured with a manifest cylinder of ≥ 0.50 D will receive a sphero-cylindrical treatment while eyes with <0.50 D of manifest cylinder will receive only a spherical treatment. Subjects implanted with the RxSight LAL will return 3 to 7 days after their first adjustment and the same measurements performed again. [redacted]

[redacted] Subjects will receive one to three adjustments and up to two lock-in treatments. All light treatments are separated by 3 to 7 days.

Postoperatively, all subjects will undergo complete ophthalmic examinations at regular intervals over a 6-month period. Masked examiners will be utilized at postop week 3 and postop month 6 to perform visual acuity and manifest refraction measurements. If a study eye is diagnosed with UV retinal damage, an additional follow-up exam will be added at 12 months postoperatively to confirm resolution or document sequelae, if any.

Subjects should be screened for eligibility and only eyes meeting all inclusion and none of the exclusion criteria will qualify for implantation. Only one eye per subject may be included in the study. At any time, the fellow eye may be implanted with any commercially available IOL including the RxSight LAL.

**INCLUSION CRITERIA**

- Must sign a written Informed Consent form and be willing to undergo cataract surgery for the implantation of an IOL with random assignment to either the RxSight LAL or the monofocal control IOL.
- Between the ages of 40 and 80 inclusive on the day the cataract surgery is performed.
- Preoperative corneal cylinder ≥0.75 diopters (D) to ≤2.00 D or >2.00 D and ≤ 2.5 D of corneal cylinder with a steep axis between 70 degrees and 110 degrees.
- Study eye has best corrected distance visual acuity projected (by clinical estimate based upon past ocular history and retinal exam) to be 20/20 or better after cataract removal and IOL implantation.
- Study eye has clear intraocular media other than cataract.
- Willing and able to comply with the requirements for study specific procedures and visits.
- Study eye has average dilated pupil diameter of ≥7.0 mm.
- Able to complete a written questionnaire in English.
- Study eye requires an IOL power within the range available for the RxSight LAL.

**EXCLUSION CRITERIA**

- Study eye with pre-existing macular disease.
- Study eye with a history of uveitis.
- Study eye with corneal pathology or corneal dystrophy that is either progressive or sufficient to reduce BCDVA to worse than 20/20.
- Subjects with serious co-morbid conditions that in the judgment of the investigator makes inclusion in the study not in the best interest of the subject.

[redacted]

*Other Key Safety parameters*

- Rates of erythropsia at each visit beginning at Postop Week 3, as evaluated by the in-office erythropsia assessment, in RxSight LAL eyes
- Rates of erythropsia at each visit beginning at Postop Week 3, as evaluated by the Daily Life Erythropsia Questionnaire (DLEQ), in RxSight LAL eyes
- Rates of tritan anomaly on the City University Color Test at each visit beginning at Postop Week 3, in RxSight LAL eyes
- Rates of all types of adverse events, including loss of best corrected distance visual acuity (BCDVA) of ≥2 lines from Postop Week 3 visit, in RxSight LAL eyes
- In specular microscopy sub-study compared between the RxSight LAL and Control group:
  - Rate of within-eye loss of ≥25% ECD from preoperative visit at Postop Week 3 and Postop Month 6
  - Rate of within-eye loss of ≥30% ECD from preoperative visit at Postop Week 3 and Postop Month 6
- Rates of findings on [redacted] testing consistent with ultraviolet retinal damage per an independent expert
- Rates of findings on [redacted] testing consistent with ultraviolet retinal damage per an independent expert

Subjects who agree to participate in the study will return for the listed follow-up examinations for the study eye:

**Examination Schedule:**

| Evaluation | RxSight LAL | Control |
|---|---|---|
| Preoperative | Day -60 to Day -1 | Day -60 to Day -1 |
| Operative | Day 0, day of surgery | Day 0, day of surgery |
| Postop Day 1 | Days 1 to 2 postop | Days 1 to 2 postop |
| Postop Week 1 | Days 7 to 14 postop | Days 7 to 14 postop |
| Postop Week 3 | Days 17 to 24 postop: Adjustment #1 | Days 17 to 24 postop |
| Adjustment #2, if needed | 3 to 7 days post Adjustment #1 | |
| Adjustment #3, if needed | 3 to 7 days post Adjustment #2 | |
| Lock-in #1 | 3 to 7 days post final adjustment | |

[1] Chen KC, Jung JJ, Aizman A. Solar Retinopathy: Etiology, Diagnosis, and Treatment. Retinal Physician, Volume 10, Issue: October 2013, pages 46-50.

| | | |
|---|---|---|
| Lock-in #2, if needed | 3 to 7 days post lock-in #1 | [redacted] |
| Postop Months 1-2 | 7 to 14 days post final lock-in visit | Days 30 to 60 postop |
| Postop Month 6 | Days 120 to 180 postop | Days 120 to 180 postop |
| Postop Month 12, if needed | Days 330 to 420 postop | [redacted] |

**Clinical Parameters:**

Clinical assessments when indicated will be performed in the following order:

1. Demographics
2. Daily Life Erythropsia Questionnaire (DLEQ) (RxSight LAL only)
3. Ocular history
4. History of Medications
5. Corneal Keratometry
6. Specular Microscopy (substudy)
7. Uncorrected distance visual acuity (UCDVA)
8. Manifest Refraction
9. Best corrected distance visual acuity (BCDVA)

[redacted]

13. Intraocular pressure
14. Slit Lamp Examination
15. Fundus Exam
16. Fundus Photos

[redacted]

18. Dilated pupil diameter

[redacted]

20. Adverse Events

## ABBREVIATIONS AND DEFINITION OF TERMS

| | |
|---|---|
| AE | Adverse Event |
| ANSI | American National Standards Institute |
| BCDVA | Best Corrected Distance Visual Acuity |
| CFR | Code of Federal Regulations |
| CI | Confidence Interval |
| CRF | Case Report Form |
| D | Diopter |
| DLEQ | Daily Life Erythropsia Questionnaire |
| ECC | Endothelial Cell Count |
| ECD | Endothelial Cell Density |
| [redacted] | [redacted] |
| ETDRS | Early Treatment Diabetic Retinopathy Study |
| FDA | Food and Drug Administration |
| GCP | Good Clinical Practice |
| ICH | International Conference on Harmonization |
| IDE | Investigational Device Exemption |
| IOL | Intraocular Lens |
| IOP | Intraocular Pressure |
| IRB | Institutional Review Board |
| LAL | Light Adjustable Lens |
| LDD | Light Delivery Device |
| M | Month |
| MR | Manifest Refraction |
| MRCYL | Manifest Refraction Cylinder |
| MRSE | Manifest Refraction Spherical Equivalent |
| OCT | Optical Coherence Tomography |
| OD | Right eye |
| OS | Left eye |
| PAS | Post-Approval Study |
| PCO | Posterior Capsular Opacity |
| PI | Principal Investigator |
| SAE | Serious Adverse Event |
| SD | Standard Deviation |
| SE | Spherical Equivalent |
| [redacted] | [redacted] |
| UADE | Unanticipated Adverse Device Effect |
| UCDVA | Uncorrected Distance Visual Acuity |

# 2 BACKGROUND

## 2.1 REGULATORY HISTORY

A Phase III clinical study conducted under IDE G100240 was a 600 eye prospective, randomized, controlled, multi-center clinical trial of the LAL and LDD designed to evaluate safety and effectiveness over a 12-month period conducted at 17 sites. In addition to the visual correction of aphakia, reduction in residual spherocylindrical refractive error and improvement in uncorrected visual acuity were evaluated following LAL implantation and subsequent refractive adjustment of the LAL by the LDD.

Eyes with ≥0.75 and ≤2.5 diopters (D) of keratometric cylinder were randomly assigned to receive either the LAL or a commercially available, posterior chamber, non-accommodating, control monofocal IOL. Six hundred eyes were implanted with 403 eyes randomized to the LAL group and 197 eyes to the Control group.

Co-primary effectiveness endpoints included percent reduction in manifest cylinder, percent mean absolute reduction in manifest refraction spherical equivalent (MRSE), and rotation of the LAL. All primary effectiveness endpoints compared pre-adjustment (LAL) or 17-21 days (Control) to 6 months postoperatively and the first two endpoints compared results between the LAL and Control groups. All three co-primary effectiveness endpoints were met with a p-value <0.0001. The difference in means for percent reduction in manifest cylinder was 54.7%, with a p-value <0.0001. The difference in means for percent reduction in absolute MRSE was 41.1% with a p-value <0.0001. Rotation of the LAL of ≤5 degrees was observed in 96.1% of LAL implanted eyes with both the upper and lower bound of the 95% confidence interval exceeding the requirement of 90%.

100% of eyes in both the LAL and Control groups had BSCVA of 20/40 or better, exceeding the historic grid rate of 92.5% (ISO 11979-7). The incidence of sight-threatening complications and adverse events for the LAL and Control groups were also below the threshold rates calculated from the 1-year historical grid for intraocular lenses (ISO 11979-7, Ophthalmic implants-Intraocular lenses- Part 7: Clinical investigations) except for the category of Secondary Surgical Interventions (SSI), which was significantly higher than the historical rate (p<.05).

On November 22, 2017, the Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) approved RxSight's premarket approval application (PMA) for the Light Adjustable Lens (LAL) and Light Delivery Device (LDD) system. The approval order included a requirement to conduct a post-approval study to evaluate the following postmarket questions:

1. What is the rate of Endothelial Cell Density loss (ECL) for patients with the LAL/LDD?
2. What is the rate of retinal damage caused by UV treatment with the LDD that may not be detected by routine post-operative testing?

The objective of this study is to address both of the postmarket safety questions.

Phase A of the study is designed to develop and validate a patient-reported outcome measure for erythropsia, the "Daily Life Erythropsia Questionnaire" (DLEQ). As this PRO instrument will be used in RxSight Investigational Device Exemption applications for the LAL and LDD as well as in Phase B of this post-approval study, RxSight submitted a Pre-Submission which provided the study protocol for development of the DLEQ to FDA on January 12, 2018 ([redacted]). As this development work is being conducted outside of the United States where the LAL and LDD are commercially available, the Pre-Submission process was thought to be the best regulatory mechanism for receiving feedback regarding the proposed development plan. [redacted] The Phase A study was completed, submitted to FDA in P160055/R003 and approved by FDA on October 24, 2019.

[redacted]

## 2.2 DEVICE DESCRIPTION

RxSight's Light Adjustable Lens (RxSight LAL) is a silicone intraocular lens whose shape and focusing characteristics can be modified after implantation using an office-based UV light source, the RxSight Light Delivery Device (LDD), to improve uncorrected distance visual acuity.

### 2.2.1 RXSIGHT LIGHT ADJUSTABLE INTRAOCULAR LENS

The RxSight LAL is a posterior chamber, UV absorbing, three-piece, foldable, photoreactive silicone intraocular lens with a squared posterior optic edge intended to be implanted in the capsular bag following phacoemulsification. Selective exposure of the implanted RxSight LAL using the LDD to deliver spatially profiled UV light produces modifications in the lens curvature resulting in a spherical or spherocylindrical power change post-operatively. A subsequent lock-in exposure is delivered to the implanted RxSight LAL to stabilize the lens power.

**Lens Optic**

- Material: Photo-reactive UV absorbing Silicone
- Light transmission: UV cut-off at 10% T ≥392 nm for all lens powers
- Index of refraction: 1.43
- Diopter power: +4.0 to +15.0 diopters and +25.0 to +30.0 D in 1.0 diopter increments; +16.0 to +24.0 diopters in 0.5 diopter increments
- Optic type: Biconvex

- Optic edge: Square on posterior surface and round on anterior surface
- Overall diameter: 13.0 mm
- Optic diameter: 6.0 mm

**Haptics**

- Configuration: Modified C
- Material: Blue core polymethylmethacrylate
- Haptic angle: 10°

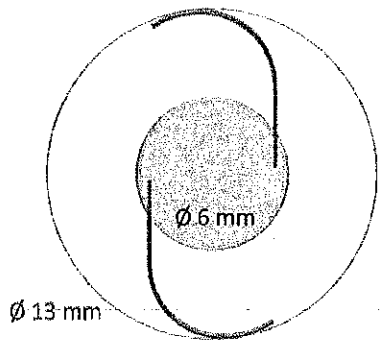


FIGURE 1: RXSIGHT LIGHT ADJUSTABLE LENS

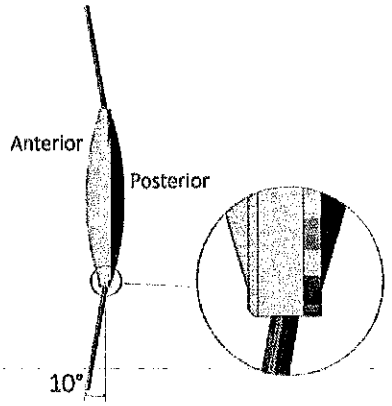


FIGURE 2: RXSIGHT LIGHT ADJUSTABLE LENS. INSET DEPICTS BACK LAYER.

The RxSight LAL silicone material is designed to respond to a narrowband UV light of a select spatial intensity profile. The silicone material contains photoreactive additive, which is selectively photo-polymerized in targeted areas upon exposure to the near UV light to alter the lens shape thus modifying spherical and spherocylindrical power of the RxSight LAL.

### 2.2.2 LIGHT DELIVERY DEVICE (LDD)

The Light Delivery Device is a digital UV light projection system used to induce a predictable change in the RxSight LAL power after implantation. The LDD consists of an anterior segment biomicroscope with the addition of an optical projection system, electronic control circuitry, and a UV source. The LDD device can treat postoperative manifest cylinder from -0.50 D to -2.00 D, and manifest sphere (in minus cylinder format) of -2.00 D to +2.00 D.

### 2.3 INDICATIONS FOR USE

The Light Adjustable Lens and Light Delivery Device system is indicated for the reduction of residual astigmatism to improve uncorrected visual acuity after removal of the cataractous natural lens by phacoemulsification and implantation of the intraocular lens in the capsular bag, in adult patients:

- With pre-existing corneal astigmatism of ≥ 0.75 diopters
- Without pre-existing macular disease.

The system also reduces the likelihood of clinically significant residual spherical refractive errors.

## 3 STUDY OBJECTIVE

The primary objective of this study is to conduct a post-approval study which evaluates the following two safety questions:

1. What is the rate of Endothelial Cell Density loss (ECL) for patients with the RxSight LAL/LDD?
2. What is the rate of retinal damage caused by UV treatment with the LDD that may not be detected by routine post-operative testing?

## 4 STUDY DESIGN

This is a two phased study that will include Phase A (complete) and Phase B.

Phase A

The primary objective of Phase A was to develop a patient-reported outcome (PRO) instrument that assessed erythropsia after LDD light treatments, the "Daily Life Erythropsia Questionnaire" (DLEQ). This was a non-interventional, cross-sectional study at 1-3 sites with primary data collection from patients who had undergone cataract surgery with implantation of the RxSight LAL and had treatment performed with the Light Delivery Device. Phase A was designed to use approximately [redacted] English speaking patients at sites in the European Union where the device has a CE Mark.

Qualitative research interviews were conducted with adult patients who reported experiencing erythropsia to their eye care provider after treatment with the Light Delivery Device. These patients were identified, invited to participate, and interviewed within 8 weeks of a report of the erythropsia symptom. Cognitive debriefing methods were used during the interviews: (1) to ensure the questionnaire captures relevant aspects of erythropsia from the patient perspective, (2) to evaluate the clarity of each question, and (3) to assess response options for each question to ensure options capture the range of patient experiences (e.g., frequency, light conditions). Cognitive interviews and qualitative coding were to be conducted in up to three rounds of interviews and analysis with about eight patients per round. This allowed an iterative approach to

the cognitive interviews and instrument modification: the DLEQ was tested with patients in the first round of interviews; following participant feedback modifications were made to the DLEQ; the revision was tested in the second round of patient interviews; based on participant feedback adjustments were made to the instrument. An optional third and final round of interviews was determined not to be need as further as further changes were not required. The instrument was revised to incorporate patients' words to support its content validity and to increase the clarity and understandability of items that will be used to assess patient experiences with erythropsia.

There will be no assessments of treatment effectiveness or safety associated with the phase for PRO development. There were no laboratory assessments associated with this research. This protocol was submitted to an Institutional Review Board(s)/Ethics Committee as required for studies with primary data collection from patients.

Patients treated in a commercial setting were evaluated using the following inclusion/exclusion criteria.

**INCLUSION CRITERIA**

- Adult patients (40 to 80 years of age) that had implantation of the RxSight Light Adjustable Lens (LAL™).
- Patient reported experiencing erythropsia to their eye care provider after treatment with the Light Delivery Device within the past eight weeks.
- Patient is able to read, write, speak, and understand English.
- Patient is willing and able to comprehend and sign a written informed consent prior to study entry.

**EXCLUSION CRITERIA**

- Patient has a clinically-relevant medical or psychiatric condition which, in the opinion of the investigator and/or coordinator, would interfere with completing the study including, but not limited to, sensory problems, cognitive impairment, acute mental illness or inadequately treated depression or anxiety.
- Complications during cataract surgery that would complicate evaluation of the erythropsia symptom.

Phase B

Phase B is a prospective, randomized, controlled, multicenter, post approval study of the RxSight LAL and LDD to be conducted at up to 15 clinical sites. It will begin after development of the "Daily Life Erythropsia Questionnaire" PRO is complete and has been accepted by FDA. This is a new enrollment study that includes up to 12 study visits. Subjects will be randomized in a 2:1 ratio to receive either the RxSight LAL or a monofocal IOL (Control).

Patients who require cataract extraction and intraocular lens implantation will be screened for eligibility. If it is determined that the patient may be eligible to participate, study staff will explain the study purpose, procedures, risks/benefits and subject responsibilities to the potential

participant. Written informed consent will be obtained prior to any study specific testing. The patient is enrolled upon signing the informed consent.

Subjects with preoperative corneal astigmatism of ≥0.75 D, without pre-existing macular disease, and meeting all inclusion/exclusion criteria will be randomly assigned in a 2:1 ratio to receive either the RxSight LAL or a commercially available monofocal IOL (Control).

Commencing at the Postop Week 3 visit, eyes will be refracted and undergo visual testing. Eyes implanted with the RxSight LAL will receive a power adjustment based on the manifest refraction. Eyes measured with a manifest cylinder of ≥ 0.50 D will receive a sphero-cylindrical treatment while eyes with <0.50 D of manifest cylinder will receive only a spherical treatment. Subjects implanted with the RxSight LAL will return 3 to 7 days after their first adjustment and the same measurements performed again. [redacted] Subjects will receive one to three adjustments and up to two lock-in treatments. All light treatments are separated by 3 to 7 days.

Postoperatively, all subjects will undergo complete ophthalmic examinations at regular intervals over a 6-month period. Masked examiners will be utilized at postop week 3 and postop month 6 to perform visual acuity and manifest refraction measurements. If a study eye is diagnosed with UV retinal damage, an additional follow-up exam will be added at 12 months postoperatively to confirm resolution or document sequelae, if any.

# 5 OUTCOME PARAMETERS

## 5.1 EFFECTIVENESS PARAMETER

The primary effectiveness endpoints are:

- Mean absolute manifest refraction spherical equivalent (|MRSE|) at postop month 6 compared between the RxSight LAL and Control group
- Mean manifest cylinder at postop month 6 compared between the RxSight LAL and Control group

The comparisons will be made by descriptive statistics only.

## 5.2 SAFETY PARAMETERS

The primary safety endpoints are:

- Median rate of endothelial cell density loss at postop month 6 compared to preoperatively compared between the LAL and Control group
- Percent of LAL eyes with UV retinal damage at postop month 6

*Other Key Safety parameters*

- Rates of erythropsia at each visit beginning at Postop Week 3, as evaluated by the in-office erythropsia assessment, in RxSight LAL eyes
- Rates of erythropsia at each visit beginning at Postop Week 3, as evaluated by the Daily Life Erythropsia Questionnaire (DLEQ), in RxSight LAL eyes
- Rates of tritan anomaly on the City University Color Test at each visit beginning at Postop Week 3, in RxSight LAL eyes
- Rates of all types of adverse events, including loss of best corrected distance visual acuity (BCDVA) of ≥2 lines from Postop Week 3 visit, in RxSight LAL eyes
- In specular microscopy sub-study compared between the RxSight LAL and Control group:
  - Rate of within-eye loss of ≥25% ECD from preoperative visit at Postop Week 3 and Postop Month 6
  - Rate of within-eye loss of ≥30% ECD from preoperative visit at Postop Week 3 and Postop Month 6
- [redacted]

## 6 STUDY POPULATION

The Phase B study will include 500 subjects who will be randomized 2:1 to receive either an RxSight LAL or a monofocal control IOL.

Subjects should be screened for eligibility and only eyes meeting all inclusion and none of the exclusion criteria will qualify for implantation.

### 6.1 INCLUSION CRITERIA

- Must sign a written Informed Consent form and be willing to undergo cataract surgery for the implantation of an IOL with random assignment to either the RxSight LAL or the monofocal control IOL.
- Between the ages of 40 and 80 inclusive on the day the cataract surgery is performed.
- Preoperative corneal cylinder ≥0.75 D to ≤2.00 D or >2.00 D and ≤ 2.5 D of corneal cylinder with a steep axis between 70 degrees and 110 degrees.
- Study eye has best corrected distance visual acuity projected (by clinical estimate based upon past ocular history and retinal exam) to be 20/20 or better after cataract removal and IOL implantation.
- Study eye has clear intraocular media other than cataract.
- Willing and able to comply with the requirements for study specific procedures and visits.

- Study eye has average dilated pupil diameter of ≥7.0 mm.
- Able to complete a written questionnaire in English.
- Study eye requires an IOL power within the range available for the RxSight LAL.

## 6.2 EXCLUSION CRITERIA

- Study eye with pre-existing macular disease.
- Study eye with a history of uveitis.
- Study eye with corneal pathology or corneal dystrophy that is either progressive or sufficient to reduce BCDVA to worse than 20/20.
- Subjects with serious co-morbid conditions that in the judgment of the investigator makes inclusion in the study not in the best interest of the subject.
- Subjects taking systemic medication that may increase sensitivity to UV light such as tetracycline, doxycycline, psoralens, amiodarone, phenothiazines, chloroquine, hydrochlorothiazide, hypericin, ketoprofen, piroxicam, lomefloxacin, and methoxsalen. LDD treatment in patients taking such medications may lead to irreversible phototoxic damage to the eye. This is only a partial list of photosensitizing medications. Please evaluate all medications that the patient is taking for this effect prior to consideration for implantation.
- Subjects taking a systemic medication that is considered toxic to the retina such as tamoxifen.
- Study eye with history of ocular herpes simplex virus.
- Study eye with nystagmus.
- Study eye that has been compromised due to previous trauma or developmental defects in which appropriate support of the intraocular lens (IOL) is not possible.
- Study eye with current vitreoretinal disease or is at a high risk for future vitreoretinal disease that may require silicone oil as part of therapy.
- Study eyes where the posterior capsule nor the zonules are intact enough to provide support for the IOL.
- Study eyes where the investigator believes maintaining study fixation will not be possible.

## 6.3 SUBJECT ENTRY

Patients who require cataract extraction and intraocular lens implantation will be screened for eligibility. If it is determined that the patient may be eligible to participate, study staff will explain the study purpose, procedures, risk/benefits and subject responsibilities to the potential participant. Written informed consent will be obtained prior to any study specific testing. The patient is enrolled upon signing the informed consent. The subject will sign and date the informed consent form in the presence of the person conducting the consent process. The investigator and/or the person conducting the consent process will also sign and date the consent form. The preoperative examination will be performed no more than 60 days prior to surgery. If the 60-day time period elapses, it is acceptable for patients to be re-screened by undergoing a complete preoperative examination.

Only subjects meeting all inclusion/exclusion criteria will be implanted. Those subjects who do not meet the inclusion/exclusion requirements will be considered screen failures. Subjects will continue to be enrolled until 500 subjects have been randomized and undergone implantation with the RxSight LAL or a monofocal IOL. If surgical complications occur and no LAL is implanted, the subject is exited from the study. Unique identification numbers will be assigned to each subject. The randomization schedules for each site will be prepared in advance and only the study statistician will have access to the randomization schedule. Prior to the surgical procedure, study site personnel will enter the subject's study ID into the study's EDC system and the treatment assignment (RxSight LAL or Control IOL) will be generated. Documentation of the randomization assignment for each subject will be maintained in the subject's file and in the EDC system.

The implant lens power for the RxSight LAL and the Control IOL will be calculated based upon the ocular biometry data and a standard IOL power calculation formula with the IOL closest to the post-surgical refractive target selected in an unbiased manner.

## 6.4 LAL IMPLANTATION AND REFRACTIVE ADJUSTMENT

### 6.4.1 SURGICAL PROCEDURE

The LAL will be implanted using standard microsurgical techniques.

No additional corneal refractive procedures are allowed until after the subject has been exited from the study.

The surgical procedure should be performed as follows:

1. Prepare and drape the eye for surgery in accordance with standard surgical procedures.
2. A clear corneal incision will be made using the surgeon's standard instrumentation and techniques.
3. Use viscoelastic to fill the anterior chamber through the incision opening.
4. Perform an anterior circular capsulorhexis [redacted] using standard technique. The capsulorhexis should be well-centered with a 360° overlapping capsular edge to minimize IOL tilt and decentration and longitudinal IOL shift. The capsulorhexis and/or nuclear fragmentation can be performed with a femtosecond laser. Precision pulse capsulotomy (PPC) can also be used to perform the capsulorhexis.
5. The surgeon will extract the cataract by phacoemulsification.
6. In the event of an intraoperative complication prior to implantation of the RxSight LAL, including posterior capsule rupture, zonular rupture, radial capsulorhexis tear, vitreous loss, iris trauma, corneal complications or any intraoperative abnormality that may affect the postoperative pupillary dilation, or the centration or tilt of the intraocular lens, do not implant the RxSight LAL.

7. The RxSight LAL will be introduced into the eye using the RxSight Insertion Device through a clear temporal corneal incision [redacted]
8. Verify proper orientation of the RxSight LAL.
9. Aspirate any residual viscoelastic from the eye using a preferred technique.
10. The wound may close without suturing. If the unsutured wound is not watertight, close it with either a suture using standard technique or an ocular sealant (ReSure Sealant).
11. After completion of the surgery, ocular anti-inflammatory and/or antibiotic drops may be applied in accordance with standard clinical practice.
12. The subject will be provided with RxSight approved UV protective spectacles to protect the implanted RxLAL from extraneous sources of UV light. It is important to direct the subject to follow all instructions that are provided with the UV protective spectacles.

    If a patch was used at the conclusion of surgery, the subject will wait for the surgeon to remove the patch. Once removed, the subject will begin wear of the UV protective eyewear as instructed.

### 6.4.2 LIGHT TREATMENT PROCEDURE

Seventeen (17) to 24 days after surgery, the subject will return for the Postop Week 3 evaluation and a 1st adjustment treatment of the RxSight LAL. Subsequent second and third adjustment treatments, if necessary, will all be separated by 3-7 days. The subject will receive the 1st lock-in treatment 3-7 days after the final adjustment treatment. If necessary, lock-in #2 may be performed 3-7 days after lock-in #1. Depending on the adjustment(s) performed, subjects will receive one to three adjustments and one or two lock-in treatments.

#### 6.4.2.1 Postponement of Light Treatment Procedure(s)

LDD treatment should be delayed if any of the following new symptoms or changes in performance are noted;

- Color Vision Testing: Treatment should be delayed if the subject scores worse on Part 2 of the City University Color Test than the Pre-adjustment test for Tritan evaluation.
- Erythropsia Evaluation: With any score of 2 (red), the treatment should be delayed.
- Best Corrected Distance Visual Acuity: With any loss of BCDVA (unless the cause is known to be non-retinal) of 10 letters or more on an ETDRS (logMAR) chart compared to the Postop Week 3 BCDVA, treatment should be delayed.

[redacted]

[redacted]

- [redacted]

[redacted]

- [redacted]

[redacted]

- [redacted]

[redacted]

- [redacted]

[redacted]

#### 6.4.2.2 Requirements for Additional Testing

Additional testing should be performed as soon as possible to evaluate whether UV-related retinal damage has occurred if any of the following is observed. [redacted] will be performed in eyes that meet any of the following criteria:

- Significant erythropsia during in office erythropsia assessment (score of 2 (red))
- Significant erythropsia as indicated on responses to the Daily Life Erythropsia Questionnaire including:
  - "severe" or "very severe" erythropsia on question 3, OR
  - a response of "very bothersome" erythropsia on question 6, OR
  - a response of "more than 7 days" on question 2
- Significant erythropsia as interpreted by the investigator based on spontaneous reports by the subject
- If the subject reports any level of erythropsia at the Postop Month 1-2 visit OR at any interim visit after the Postop Month 1-2 visit and <90 days after surgery based on results of the in office erythropsia assessment, the Daily Life Erythropsia Questionnaire or spontaneous verbal reports by the subject, the subject will be mailed a paper version of the Daily Life Erythropsia Questionnaire to self administer and return to the investigational site between 90-120 days after surgery. If responses to the Daily Life

[2] Azar D, Stark W, Dodick J, et al. Prospective, randomized vector analysis of astigmatism after three-, one-, and no-suture phacoemulsification. J Cataract Refract Surg 1997; 23:1164-1173.

Erythropsia Questionnaire indicate that there is erythropsia on question 1, the subject should have an unscheduled visit and testing should be performed.

- Any level of erythropsia at any unscheduled visit at 3-months or later or at the Postop Month 6 based on results of the in office erythropsia assessment, the Daily Life Erythropsia Questionnaire or spontaneous verbal reports by the subject
- Has a tritan anomaly (tritan score >1 on Part II of the 3rd Edition City University Color Vision Test (CUT) when tritan score was 0 pre-treatment) or an increase in tritan score of >1 at any time after light treatment
- Has an unexplained loss of best corrected distance visual acuity ≥2 lines compared to pre-light-treatment at any visit (scheduled or unscheduled) after the first light treatment
- [redacted]

[redacted]

[redacted] testing should be repeated at subsequent study visit(s) following the diagnosis of retinal phototoxicity to assess subsequent changes. If a study eye is diagnosed with UV retinal damage, an additional follow-up exam will be added at 12 months postoperatively. Diagnostic imaging/testing of the fellow eye may be performed if in the opinion of the investigator additional information will aid in evaluation or diagnosis.

### 6.4.2.3 Procedure Preparation

Protocol-required measurements should be completed prior to adjustment or lock-in treatments.

The subject should be prepared for light treatments as follows:

1. [redacted]
2. Once adequate pupil dilation is achieved, patch the subject's fellow eye and position the subject comfortably in front of the LDD with chin in the chinrest and forehead against the support bar. Ask the subject to grasp the handles on the LDD table for support. Inform the

subject to concentrate on the green fixation light presented in front of them and to try and minimize eye movement.

#### 6.4.2.4 Adjustment Procedure(s)

Refer to the LDD Operator's manual for instructions on LDD start up and instructions for the daily alignment test to be performed prior to the first treatment of the day to ensure the UV beam is aligned to the reticle. If the UV beam is not aligned to the reticle within the specifications detailed in the LDD Operator's manual, do not perform treatments and call RxSight customer service immediately.

1. All adjustment procedure(s) will be recorded.
2. Within the Patient ID and Patient Data screens, follow the touchscreen prompts to enter requested information. Press the "Proceed" button once information has been entered respectively for each screen.
3. Within the Confirmation screen, review all information and press the "Confirm" button.
4. Verify that the LDD ring lights and reticle target are activated.
5. Apply topical anesthetic.
6. Position the RxSight supplied contact lens (M = 0.766x) on the cornea using hydroxypropyl methylcellulose as the coupling medium.

**Note:** The RxSight contact lens is similar to those used in other ophthalmic procedures in which customized magnification is required. To ensure correct magnification for treatment, use only the RxSight designated contact lens.

7. Instruct the subject to focus straight ahead on the LDD fixation light with the study eye.
8. Using the microscope, focus on the cornea and verify that there are no trapped bubbles present. Confirm alignment of the contact lens by approximately aligning the Purkinje images to the inner circle of the reticle target.
9. Using the microscope, focus on the RxSight LAL haptics and align the reticle target with the periphery of the RxSight LAL.
10. Press the "Ready" button
11. Initiate the UV exposure as prompted by the LDD display using the trigger. Use the joystick to keep the RxSight LAL centered in the alignment reticle.
12. Perform micro adjustments to keep the reticle target centered to the RxSight LAL and to keep the RxSight LAL in focus. In the case of subject movement, loss of alignment, or loss of focus, pause the treatment, quickly refocus, realign the lens with respect to the reticle beam, and immediately resume treatment to limit the duration of any pauses once the light treatment has been initiated.

Note: Always maintain the RxSight LAL in focus by focusing at the haptics. Never focus onto the CCC (capsulotomy) or Purkinje images.

13. If the event of an aborted Adjustment Treatment, do not initiate a new treatment sequence; instead; instruct the subject to return 3-7 days later for refractive evaluation to assess whether an adjustment treatment is required or to proceed directly to a lock-in treatment.
14. Following the light adjustment, the subject will continue to wear their UV protective eyewear as instructed until exactly 24 hours after the final lock-in treatment has been completed.

    The subject will return 3 to 7 days following the power adjustment treatment for another light treatment. The subject may receive up to 3 adjustment treatments before receiving the 1st lock-in treatment.

#### 6.4.2.5 Lock-In Procedure(s)

Refer to the LDD Operator's manual for instructions on LDD start up and instructions for the daily alignment test to be performed prior to the first treatment of the day to ensure the UV beam is aligned to the reticle. If the UV beam is not aligned to the reticle within the specifications detailed in the LDD Operator's manual, do not perform treatments and call RxSight customer service immediately.

1. All lock-in procedure(s) will be recorded.
2. Within the Patient ID screen, utilize the pop-out menu within the Patient ID field to select the appropriate subject identification with eye to be treated. Reconfirm information displayed on screen and follow the touch screen prompts to enter in newly requested information. Press the "Proceed" button.
3. Within the Confirmation screen, review all information and press the "Confirm" button.
4. Verify that the LDD ring lights and reticle target are activated.
5. Apply topical anesthetic.
6. Position the RxSight supplied contact lens (M = 0.766x) on the cornea using hydroxypropyl methylcellulose or hypromellose as the coupling medium.

**Note:** The RxSight contact lens is similar to those used in other ophthalmic procedures in which customized magnification is required. To ensure correct magnification for treatment, use only the RxSight designated contact lens.

7. Instruct the subject to focus straight ahead on the LDD fixation light with the study eye.
8. Using the microscope, focus on the cornea and verify that there are no trapped bubbles present. Confirm alignment of the contact lens by approximately aligning the Purkinje images to the inner circle of the reticle target.
9. Using the microscope, focus on the RxSight LAL haptics and align the reticle target with the periphery of the RxSight LAL.
10. Press the "Ready" button

11. Initiate the irradiation delivery as prompted by the LDD display using the joystick or foot pedal to keep the RxSight LAL centered in the alignment reticle.
12. Perform micro adjustments to keep the reticle target centered to the RxSight LAL and to keep the RxSight LAL in focus. In the case of subject movement, loss of alignment, or loss of focus, pause the treatment, quickly refocus, realign the lens with respect to the reticle beam, and immediately resume treatment to limit the duration of any pauses once the light treatment has been initiated.

Note: Always maintain the RxSight LAL in focus by focusing at the haptics. Never focus onto the CCC (capsulotomy) or Purkinje images.

13. If the lock-in treatment is aborted before completion, contact the Sponsor for technical assistance.
14. Upon completion of the lock-in #1 treatment, a notification that indicates either "All required treatments complete" or "Lock-In #2 Required" will appear. If "All required treatments complete", proceed to step #16. If "Lock-In #2 Required", proceed to step #15.
15. The subject will return for the second lock-in treatment 3 to 7 days after the first lock-in treatment.
16. The subject will be permitted to discontinue wear of the UV protective eyewear exactly 24 hours after all lock-in treatments are completed.

### 6.5 CONTROL LENS IMPLANTATION

The commercially available, posterior chamber, non-accommodating monofocal IOL of the investigators choice will be implanted on Day 0 of the study. A clear corneal incision will be made using the surgeon's standard incision size, instrumentation and technique. All instruments and procedures used will be identical to those routinely used for phacoemulsification by each individual investigator.

## 6.6 EXAMINATION SCHEDULE

Subjects who agree to participate in the study will return for the listed follow-up examinations for each study eye:

| Evaluation | RxSight LAL | Control |
|---|---|---|
| Preoperative | Day -60 to Day -1 | Day -60 to Day -1 |
| Operative | Day 0, day of surgery | Day 0, day of surgery |
| Postop Day 1 | Days 1 to 2 postop | Days 1 to 2 postop |
| Postop Week 1 | Days 7 to 14 postop | Days 7 to 14 postop |
| Postop Week 3 | Days 17 to 24 postop: Adjustment #1 | Days 17 to 24 postop |
| Adjustment #2, if needed | 3 to 7 days post Adjustment #1 | |
| Adjustment #3, if needed | 3 to 7 days post Adjustment #2 | |
| Lock-in #1 | 3 to 7 days post final adjustment | |
| Lock-in #2, if needed | 3 to 7 days post lock-in #1 | |
| Postop Months 1-2 | 7 to 14 days post final lock-in visit | Days 30 to 60 postop |
| Postop Month 6 | Days 120 to 180 postop | Days 120 to 180 postop |
| Postop Month 12, if needed | Days 330 to 420 postop | |

A Postop Month 12 visit will be conducted if a subject is diagnosed with UV retinal damage to confirm resolution or document sequelae, if any.

Unscheduled visits falling outside the designated ranges for scheduled visits will be considered "interim" visits for data recording purposes and a report form will be completed.

## 6.7 CLINICAL PARAMETERS

The following study parameters will be assessed as specified in Table 1 for the RxSight LAL and Table 2 for the Control IOL. Assessments will be performed using the techniques described in [redacted] and in the order presented here and in Table 1.

1. Demographics
2. Daily Life Erythropsia Questionnaire (DLEQ) (RxSight LAL only)
3. Ocular history
4. History of Medications
5. Corneal Keratometry
6. Specular Microscopy (substudy)
7. Uncorrected distance visual acuity (UCDVA)
8. Manifest Refraction
9. Best corrected distance visual acuity (BCDVA)
10. In-office Erythropsia Assessment (RxSight LAL only)
11. City University Color Test (RxSight LAL only)
12. [redacted]
13. Intraocular pressure
14. Slit Lamp Examination
15. Fundus Exam
16. Fundus Photos
[redacted]
18. Dilated pupil diameter
[redacted]
20. Adverse Events

**Table 1. RxSight LAL Schedule of Visits and Clinical Parameters**

| Visits | Preop | Operative | Postop Day 1 | Postop Week 1 | Postop Week 3 | Adjustment #2 (if needed) | Adjustment #3 (if needed) | Lock-in #1 | Lock-in #2 (if needed) | Postop Months 1-2 | Postop Month 6 | Postop Month 12 (if needed) | Unscheduled Visit[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Demographics | X | | | | | | | | | | | | |
| Daily Life Erythropsia Questionnaire (DLEQ) | | | | | X | X | X | X | X | X[4] | X | X | X |
| Ocular History | X | | | | | | | | | | | | |
| History of Medications | X | X | X | X | X | X | X | X | X | X | X | X | X |
| Corneal Keratometry | X | | | | | | | | | | | | |
| Specular Microscopy[3] | X | | | | X | | | | | | X | | |
| Uncorrected distance visual acuity (UCDVA) | X | | X | X | M | X | X | X | X | X | M | X | X |
| Manifest Refraction | X | | | X | M | X | X | X | X | X | M | X | |
| Best corrected Visual Acuity Distance (BCDVA) | X | | | X | M | X | X | X | X | X | M | X | |
| In-office Erythropsia Assessment | | | | | X | X | X | X | X | X | X | X | X |
| City University Color Test | | | | | X | X | X | X | X | X | X | X | X[5] |
| [redacted] | | | | | X | X[1] | X[1] | X[1] | X[1] | X[1] | X[1] | X[1] | |
| Intraocular Pressure | X | | X | X | X | X | X | X | X | X | X | X | |
| Slit Lamp Exam | X | | X | X | X | X | X | X | X | X | X | X | X |
| Fundus Exam | X | | | | X | X | X | X | X | | X | X | |
| Fundus Photos | X | | | | X | X | X | X | X | | X | X | |
| [redacted] | | | | | X | X | X | X | X | X | X | X | |
| Dilated Pupil Diameter | X | | | | X | X | X | X | X | | | | |
| [redacted] | | | | | | X[1] | X[1] | X[1] | X[1] | X[1] | X[1] | X[1] | |
| Adverse Events | | X | X | X | X | X | X | X | X | X | X | X | X |

[redacted] are only required if the events described in Section 6.4.2.2 of the protocol occur.
[2]Tests indicated with an "X" must be performed at each unscheduled visit. Other tests may be conducted based on the investigator's assessment of the subject.
[3]Specular microscopy will be performed on a subgroup of approximately 300 eyes including a minimum of 192 LAL eyes and 96 Control eyes.
[4]If the subject reports any degree of erythropsia at the Postop Month 1-2 visit OR at any interim visit after the Postop Month 1-2 visit and <90 days after surgery, the subject will be contacted between 90-120 days after surgery and asked to complete the Daily Life Erythropsia Questionnaire.
[M] Measurements will be conducted by a masked observer who will not be aware of which lens has been implanted in the eye. The masked observer should not have access to the subject's medical and/or study records.
[5]Must be performed at any unscheduled visit which occurs at 3-months or later.

**Table 2. Control IOL Schedule of Visits and Clinical Parameters**

| Visits | Preop | Operative | Postop Day 1 | Postop Week 1 | Postop Week 3 | Postop Months 1-2 | Postop Month 6 | Unscheduled Visit[1] |
|---|---|---|---|---|---|---|---|---|
| Demographics | X | | | | | | | |
| Ocular History | X | | | | | | | |
| History of Medications | X | X | X | X | X | X | X | X |
| Corneal Keratometry | X | | | | | | | |
| Specular Microscopy (substudy)[2] | X | | | | X | | X | |
| Uncorrected distance visual acuity (UCDVA) | X | | X | X | M | X | M | X |
| Manifest Refraction | X | | | X | M | X | M | |
| Best corrected Visual Acuity Distance (BCDVA) | X | | | X | M | X | M | |
| Intraocular pressure | X | | X | X | X | X | X | |
| Slit Lamp Exam | X | | X | X | X | X | X | X |
| Fundus Exam | X | | | | X | | X | |
| Fundus Photos | X | | | | X | | X | |
| Dilated Pupil Diameter | X | | | | X | | | |
| Adverse Events | | X | X | X | X | X | X | X |

[1]Tests indicated with an "X" must be performed at each unscheduled visit. Other tests may be conducted based on the investigator's assessment of the subject.
[2]Specular microscopy will be performed on a subgroup of approximately 300 eyes including a minimum of 192 LAL eyes and 96 Control eyes.
[M] Measurements will be conducted by a masked observer who will not be aware of which lens has been implanted in the eye. The masked observer should not have access to the subject's medical and/or study records.

## 6.8 DATA REPORTING

Electronic data capture (EDC) will be utilized for this study. Case report forms (CRFs) will be provided by the sponsor for each eye enrolled in the study. In order to facilitate data entry, the CRFs coincide with the data entry pages in the EDC system. The appropriate CRFs will be completed and initialed or signed where indicated at each examination. All CRFs will be completed in a legible manner in black/blue ink.

Any corrections to the CRFs will be made by drawing a single line through the incorrect entry, recording the correct information, and initialing and dating the change. The study CRFs and data entered in the EDC system will be reviewed by the Study Monitor.

All clinical data generated in the study will be submitted to the RxSight Clinical Affairs Department or designated CRO for quality assurance review and statistical analysis. All CRFs and data entered into the EDC system will be reviewed for completeness and evident recording errors will be rectified by contact with the appropriate clinical site. Computerized data checks will be used to identify unusual data entries for verification prior to statistical analysis.

To minimize the amount of missing data, investigators will be trained on the deleterious effect that missing data have on trial integrity and credibility and that missing data could diminish the scientific value of all subjects' altruistic contributions.

## 6.9 STUDY COMPLETION PROCEDURES

An End of Study Form must be completed for all subjects enrolled in the study upon subject completion, withdrawal or discontinuation.

### 6.9.1 SUBJECT COMPLETION

Subjects are considered to have completed the study if they have completed the Postop Month 6 examination unless the subject is diagnosed with retinal phototoxicity. In that case, a Month 12 examination will be conducted for the RxSight LAL group only to confirm resolution or document sequelae, if any.

Subjects with ocular serious adverse events or adverse device effects that are unresolved at study exit should continue to be followed until resolution of the event or until they are stable per the investigator's evaluation.

### 6.9.2 SUBJECT WITHDRAWAL PRIOR TO IMPLANTATION

Subjects may be withdrawn from the study prior to implantation if they do not meet all inclusion/exclusion criteria (screen failures) or decide not to participate in the study.

### 6.9.3 SUBJECT WITHDRAWAL DUE TO INTRAOPERATIVE COMPLICATIONS PRIOR TO IMPLANTATION

Subjects that meet all inclusion/exclusion criteria but do not undergo implantation of the RxSight LAL due to intraoperative complications prior to introduction of the RxSight LAL will be followed to resolution of any adverse events and then exited from the study.

### 6.9.4 SUBJECT DISCONTINUATION AFTER IMPLANTATION

After implantation, subjects may not be withdrawn from the study unless the study lens has been explanted. In the case of an explant, the investigator should continue follow-up for a period that ensures no adverse consequences have resulted. When possible, all necessary clinical assessments will be performed prior to the Subject exiting the study even if the assessment was not scheduled at that particular visit.

Subjects may be discontinued from the study only when the study lens has been explanted or subject has deceased. The reason for discontinuation will be recorded on the appropriate study worksheet. Subjects who are discontinued from the study will still be a part of the study analyses up until the point they are exited.

### 6.9.5 LOST TO FOLLOW-UP

Subjects for which the final post-operative case report form is overdue and who refuse to be followed, or have difficulty being followed, or cannot be contacted despite extensive written and telephone follow-ups to determine the final clinical outcome, will be considered lost to follow-up. Sites must make a minimum of three documented attempts via telephone, email, or regular mail to contact the subject. If the subject does not reply to any of these attempts, the site must send a letter by certified mail (with a request for notification of receipt of delivery) to the subject. If a subject is non-responsive to these follow-up attempts, the subject will be considered to be lost to follow-up.

# 7 STATISTICAL METHODS

## 7.1 SAMPLE SIZE CALCULATION

The sample size calculations for the post-approval study are based on the two safety endpoints and their corresponding statistical hypotheses described below.

### 7.1.1 ENDOTHELIAL CELL DENSITY (ECD)

The endothelial cell loss (ECL) at 6 months after the cataract surgery will be compared between the LAL and Control groups.

[redacted]

[redacted]

### 7.1.2 UV RETINAL DAMAGE NOT DETECTABLE THROUGH ROUTINE CLINICAL EXAMINATIONS

[redacted]

[redacted]

## 7.2 GENERAL CONSIDERATION

The statistical analysis of the data will be performed using SAS version 9.3 or higher or another industry standard statistical software package. Continuous variables will be summarized using descriptive statistics, specifically the mean, median, standard deviation, minimum and maximum. Categorical variables will be summarized by frequencies and percentages. Safety analyses will be performed on eyes in which IOL implants are attempted.

A detailed statistical analysis plan (SAP) will be developed and finalized prior to the locking of the database for this study.

## 7.3 BASELINE CHARACTERISTICS

Baseline characteristics (such as age, gender, race, and pre-operative pathology) will be summarized descriptively by means and standard deviations or by counts and percentages, as appropriate. They will also be stratified by the study site in order to assess the similarity of these baseline characteristics among the study sites.

## 7.4 POPULATIONS FOR ANALYSIS

### 7.4.1 SAFETY POPULATION

The safety population consists of any subject who has signed the informed consent and has the procedure attempted which is defined as the point at which the lens makes contact with the eye. This population will be used for the safety. No imputation will be performed.

[3] Conover, W.J. (1980). Practical Nonparametric Statistics 2 ed. J. Wiley, New York

### 7.4.2 ENDOTHELIAL CELL POPULATION

The endothelial cell population consists of members of the safety population who are entered in the endothelial cell subgroup and have specular microscopy images taken at the preoperative examination.

### 7.4.3 EFFECTIVENESS POPULATION

The effectiveness population consists of members of the safety population who are implanted with the randomized intraocular lens and have the 6-month manifest refraction data.

## 7.5 EFFECTIVENESS ANALYSES

The following effectiveness outcomes will be summarized descriptively based on the observed data of the effectiveness population for the RxSight LAL and Control eyes separately.

[redacted]

## 7.6 SAFETY PARAMETERS

All data analyses will be based on the observed data and actual lens implanted. No imputation will be performed for the missing data.

### 7.6.1 CO-PRIMARY SAFETY ENDPOINT: PERCENT ECL FROM PREOP TO 6 MONTHS POSTOP

[redacted]

[redacted]

### 7.6.2 CO-PRIMARY SAFETY ENDPOINT: UV RETINAL DAMAGE NOT DETECTABLE THROUGH ROUTINE CLINICAL EXAMINATIONS

[redacted]

### 7.6.3 ADDITIONAL SAFETY ANALYSES

The following safety outcomes will be summarized descriptively based on the observed data and actual lens implanted. Results will be presented for all the RxSight LAL eyes and the Control group eyes. The 95% confidence intervals for means or percentage may be presented, as appropriate.

Adverse Events

Number and percent of study eyes will be summarized for each reported ocular AE at the operative visit and each postoperative visit for the LAL group and Control group separately. Serious ocular AEs and the non-ocular serious AEs will be summarized in the same manner. Additionally, for each of the device related AE reported during the study, the number and

percent of study eyes reported with the event will be presented. The ocular adverse events will be listed for eyes, if applicable, with IOL implantation attempted but without implantation. Ocular adverse events will be reported separately for the fellow eye.

BCDVA

BCDVA will be presented with the number and percent of eyes who fall into each category of BCDVA at each visit (e.g. 20/20 or better, 20/25 or better, 20/32 or better, etc.). The mean and standard deviation (SD) of BCDVA letter score will also be calculated for each visit. Change in BCDVA from Postop Week 3 or from Preoperative will be presented at each visit as categorical outcomes of "Increase in 15 letters or more", "Increase in 10-14 letters", " Increase in 5-9 letters", "No change", "Decrease in 5-9 letters", "Decrease in 10-14 letters", and "Decrease in 15 letters or more The mean and SD of the change from Postop Week 3 or Preoperative will also be presented. Similarly, the mean change from the prior visit to the next visit will also be summarized in the same manner.

In-Office Erythropsia Assessment (RxSight LAL only)

The number and percent of eyes in each outcome of erythropsia assessment (0- white, 1- pink, or 2- red) will be presented. In addition, the number and percent of eyes with increases in the level of erythropsia from the Postop Week 3 visit will be presented.

Daily Life Erythropsia Questionnaire (RxSight LAL only)

Results of the Daily Life Erythropsia Questionnaire will be summarized descriptively at each visit the questionnaire is completed.

City University Color Test (RxSight LAL only)

Results of the City University Color Test will be reported as the number and percent of eyes that have tritan findings >1 on Part Two of the test.

Slit Lamp Examinations

Slit lamp findings will be summarized descriptively.

Fundus Exam and Fundus Photos (RxSight LAL only)

Number of subjects with fundus exam changes from the pre-op and Postop Week 3 evaluation will be summarized.

[redacted]

[redacted]

### 7.6.4 ADDITIONAL ANALYSES

All other clinical outcomes will be summarized descriptively at each visit based on the observed data and actual lens implanted. Results will be presented for all the RxSight LAL eyes and the Control group eyes. The 95% confidence intervals for means or percentage may be presented, as appropriate. These clinical outcomes include uncorrected visual acuity (UCVA), manifest cylinder (MRCYL), manifest spherical equivalent (MRSE), absolute MRSE, MRCYL or MRSE within 0.50 D and 1.00 D from intended correction, change in MRCYL or MRSE or absolute MRSE from Postop Week 3, vector change in MRCYL from Postop Week 3, and Defocus Equivalent (DEQ). Additionally, the stability of MRSE and MRCYL will be summarized per Section F.3 of ANSI Z80.11-2012.

## 8 ADVERSE EVENTS

Throughout the course of the study, all efforts will be made to remain alert to possible adverse experiences or untoward findings. If adverse events occur, the first concern will be the safety and welfare of the subject and appropriate medical intervention will be made. All anticipated and unanticipated adverse events regardless of severity will be captured on the Case Report Forms (CRF) and the Adverse Event Form.

All adverse events will be evaluated by the manufacturer/study sponsor (RxSight) per the internal procedure (OP 1026) to determine if the event is reportable to FDA under 21 CFR § 803: Medical Device Reporting, Subpart E – Manufacturer Reporting Requirements. Study events meeting the definition below of an MDR reportable event will be reported to CDRH electronically via the eMDR system within the required time frames. In addition, the post approval study reports shall include a summary table of MDRs filed for this PAS study.

### 8.1 ADVERSE EVENT DEFINITIONS

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device.

Note 1 to entry: This definition includes events related to the investigational medical device or the comparator.

Note 2 to entry: This definition includes events related to the procedures involved.

*Serious Adverse Events (SAEs)* are AEs that lead to:

- death
- a serious deterioration in the health of the subject that:
  - results in a life-threatening illness or injury
  - results in a permanent impairment of a body structure or function (e.g., blindness)
  - requires in-subject hospitalization or prolongation of existing hospitalization
  - results in medical or surgical intervention to prevent permanent impairment to a body structure or a body function
- fetal distress, fetal death, or a congenital abnormality or birth defect
- a potentially sight-threatening condition
- or is another important medical event.

*MDR reportable event*: An event that manufacturers become aware of that reasonably suggests that one of their marketed devices:
• May have caused or contributed to a death or serious injury, or
• Has malfunctioned and that the device or a similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

*Serious injury* means an injury or illness that:
• Is life-threatening,
• Results in permanent impairment of a body function or permanent damage to a body structure, or
• Necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure. Permanent means irreversible impairment or damage to a body structure or function, excluding trivial impairment or damage.

The following may be considered normal events after cataract surgery and only need to be reported as AEs as specified:

- Iritis/cells/flare (if present after Postop Week 1 and greater than grade 1 (trace)) or (any iritis/cells/flare present at Postop Month 6 of any grade)
- Chronic anterior uveitis-anterior segment inflammation characterized by grade 1+ cell or greater (using the Standardization of Uveitis Nomenclature criteria) that is persistent for greater than 3 months postoperatively, or relapses in less than 3 months after discontinuation of therapy, or the subject is maintained on therapy for more than 3 months to control inflammation
- Corneal edema (corneal swelling (stromal or epithelial) (if present after Postop Week 1 and greater than grade 1 (trace)), OR resulting in BCDVA of 20/40 or worse at Postop Month 1-2 or later, OR (if present at Postop Month 6 of any grade)
- Raised intraocular pressure (IOP) >10 mmHg above preoperative and greater than 25 mmHg (if present after Postop Week 1) AND unrelated to mechanical pupillary block

In addition, the specific following events should be reported as an AE:

- An increase in score of more than 1 on Part 2 of the Tritan evaluation (City University Color Test) when compared to the Postop Week 3 score.
- An erythropsia score of 2 (red) at any time after Postop Week 3.
- An eythropsia score of 1 (pink) or (2) red at the Postop Month 6 visit.

All adverse events should be reported and information provided regarding whether the adverse event meets the above definitions.

## 8.2 IDENTIFICATION AND COLLECTION

Identification and collection of an AE begins after informed consent has been obtained and documented. Standard sources of identifying AEs include:

- direct observation by the Investigator or study team member
- asking the study participant a specific question (e.g., "Since your last visit, have you experienced any problems with your eyes or vision?")
- unsolicited volunteering of information by the study participant (e.g., "Doctor, I have had numerous headaches since I started using this lens.")

Ocular AEs and SAEs and systemic SAEs observed or elicited by the Investigator, reported by the subject, or resulting from a test result, etc., occurring during the clinical investigation must be documented. During the study, the Investigator should treat the study subject as appropriate to ensure his/her safety and welfare. Refer to Section 6.9.1 for additional information pertaining to ongoing AEs at subject exit.

Pre-existing conditions will not be considered AE/SAEs but will be collected at the Preoperative Visit as medical history. A worsening of a pre-existing condition during the study should be documented as an AE and evaluated accordingly.

Hospitalization is a criterion for assessment of seriousness. Hospitalization in the absence of a medical AE is not in itself an AE. For example, the following reports of hospitalization without a medical AE should not be considered either an SAE or an AE:

- Planned hospitalization for a pre-existing condition without serious deterioration in health (e.g., planned knee replacement surgery)
- Social admission (e.g., subject has no place to sleep)
- Administrative admission (e.g., for yearly physical exam or elective procedures not related to the study)
- Optional admission not associated with a precipitation medical AE (e.g., for elective cosmetic surgery)

## 8.3 EVALUATIONS

When evaluating AEs, the Investigator must determine if the event is serious, assess the severity of symptoms, the relationship of the event to the device or study protocol, using the following guidelines:

1. **Severity**

   **Mild**: subject awareness of a sign or symptom that is easily tolerated, requires no treatment, and does not interfere with subject's daily activities

   **Moderate:** subject awareness of a sign or symptom which may be a low level of concern to the subject and may interfere with daily activities, but can be relieved by simple therapeutic care

   **Severe:** a sign or symptom that interrupts the subject's daily activity and requires systemic therapy or other treatment

2. **Relationship (Causality) to Study Device or Study Protocol**

   **Related:** There is at least a reasonable possibility that the AE/SAE is related to the study device or study protocol. Reasonable possibility means that there is evidence to suggest a causal relationship between the study device or study protocol and the AE.

   **Unrelated:** There is little or no reasonable possibility that the AE/SAE is related to the study device or study protocol. This assessment implies that the AE/SAE has little or no temporal relationship to the study device and/or a more likely or certain alternative etiology exists.

## 8.4 SAE REPORTING

The site should report any event to the Sponsor and its representative in an expedited manner if it meets the criteria for an SAE and/or is an IOL explant from a study eye. Expedited reporting is calling or e-mailing the Sponsor and its representative within 48 hours of becoming aware of the event. When reporting an SAE to the Sponsor and/or its representative, the site should forward any supporting documents along with the SAE Report Form to the Sponsor and its designee within 5 days of the initial communication. Sites must also report these events to the reviewing IRB/IEC per its established reporting procedures.

## 8.5 PREGNANCY

During the study, all female subjects of childbearing potential should be instructed to contact the investigator immediately if they suspect they might be pregnant (e.g., missed or late menstrual period). Female subjects who become pregnant during the study will be followed until completion of pregnancy. Every effort will be made to obtain the health status of the mother and infant or fetus (in cases of miscarriage or therapeutic abortion) at term. Pregnancy itself is not considered an AE.

All confirmed pregnancies must be immediately reported to the Sponsor within 48 hours of the investigator's awareness of the pregnancy.

## 8.6 POTENTIAL ADVERSE EVENTS

The following have been identified as potential adverse events for all cataract surgeries including the RxSight LAL and the control IOL. Please notify the Sponsor regarding any events that may be occurring more frequently than your customary rates, or more frequently than expected at your site.

Infection (endophthalmitis), hypopyon, infectious keratitis, hyphema, inflammation, corneal endothelial damage, IOL dislocation out of the posterior chamber, cystoid macular edema or other retinal problems including and epiretinal membranes, toxic anterior segment syndrome, striation on the lens with or without visual sequelae, iritis, synechiae, ptosis, wound leak, flat anterior chamber, increased astigmatism, vitreous in the anterior chamber, retained pieces of the lens in the eye, corneal edema, pupillary block, retinal detachment, transient or persistent glaucoma, vitritis, iris prolapse, rupture of the capsule, and secondary surgical intervention. Increased visual symptoms related to the optical characteristics of the IOL include: halos, glare, and/or double vision.

Secondary surgical interventions include, but are not limited to: lens repositioning, lens replacement, vitreous aspirations or iridectomy for pupillary block, lysing of synechiae, wound leak repair, retinal detachment repair and corneal transplant.

These adverse events may result in total loss of vision or the loss of an eye.

Additionally, a posterior capsulotomy may be required to treat posterior capsular haze after the cataract surgery. These and other complications may result in permanent poor vision.

[redacted]

# 9 STUDY MONITORING

RxSight clinical personnel or designated CRO will monitor all clinical studies in a manner consistent with any applicable health authority regulations and the clinical research standards adopted by RxSight's Clinical Affairs Department. Study monitoring will involve the following elements:

- Member(s) of RxSight's Clinical Affairs Department or designated CRO may meet with investigators prior to the initiation of the study in order to review the adequacy of the subject population, facilities, and equipment with respect to the needs of the study, and to familiarize the investigator with the study protocol. This evaluation may be performed remotely.
- A member of RxSight's Clinical Affairs Department or designated CRO may meet with the investigator(s) at the time study subjects begin to be enrolled in order to ensure that subjects are being properly selected and that study data are being correctly recorded. These meetings and assessments may be performed remotely.
- A member of RxSight or designated CRO may visit the clinical site at any time during the study to review study worksheets and data entered in the EDC system. Remote review of study worksheets, case histories and other data (including data with PHI) may be reviewed remotely.
- Interim monitoring visits and telephone consultations will occur as necessary during the course of the study to ensure the proper progress and documentation of the study findings. Centralized and/or remote monitoring may be performed during the conduct of the study. Interim monitoring visits may be performed remotely; this includes remote review of study worksheets, case histories and other data which may contain PHI.
- RxSight clinical personnel may visit the site at any time during the course of the study to observe implantation of the RxSight LAL and the adjustment and lock-in treatments to ensure that the procedures described in the protocol are being followed. Visits by RxSight clinical personnel may occur via video conferencing.
- RxSight clinical personnel may also observe examination techniques used by study personnel to ensure that the procedures being utilized are the procedures described in [redacted]. RxSight clinical personnel may also observe examination techniques via video conferencing.

# 10 ETHICAL AND REGULATORY CONSIDERATIONS

## 10.1 SUBJECT INFORMATION AND CONSENT

It is the responsibility of the Principal Investigator or authorized designee to give each subject prior to inclusion in the study full and adequate verbal and written information regarding the objective and procedures of the study and the possible risks involved. The subjects will be informed about their right to refuse to participate in the study. The written consent form will be given to each subject before enrollment. It is the responsibility of the Principal Investigator to obtain a signed informed consent form and a HIPAA consent form and to ensure the subject is given a copy of each.

The Principal Investigator or authorized designee needs to file the informed consent forms for review by RxSight study monitors. The Investigator or authorized designee will acknowledge the receipt of the informed consent form from each subject by signing the appropriate pages of these documents.

## 10.2 DECLARATION OF HELSINKI

The study will be performed in accordance with the relevant recommendations guiding physicians in biomedical research involving human subjects adopted by the 18th World Medical Assembly, Helsinki, Finland, 1964 and later revisions, as well as applicable U.S. Food and Drug Administration regulations (21 CFR Parts 50, 56, and 812).

It is the responsibility of the Principal Investigator to obtain Institutional Review Board approval of the Study Protocol and to keep the IRB informed of serious side effects or adverse events and any amendments to the protocol.

## 10.3 ADDITIONAL REGULATORY CONSIDERATIONS

The proposed study is subject to all applicable governmental rules and regulations concerning the conduct of clinical trials on human subjects. This includes, but is not necessarily limited to, the approval of an Institutional Review Board (where applicable); obtaining prospective informed consent; monitoring of the conduct of the study, the completeness of the study worksheets, and accuracy of data entered into the EDC system, as may be employed, by the Sponsor or its designee(s); and record retention by the Sponsor in accordance with 21 CFR Subpart G-Records and Reports.

# 11 REPORTING REQUIREMENTS

An interim report will be submitted every 6 months for the first 2 years of the study and then annually thereafter, from the date of the approval of the PMA Supplement. The interim analyses will be posted on the FDA post-approval website for public access. Descriptive analyses will be provided including subject enrollment, demographic data, follow-up rate, and summary measurements for safety and effectiveness defined the same as in the final report.

## 12 STUDY MILESTONES/

[redacted]

## 13 REFERENCES

1. Chen KC, Jung JJ, Aizman A. Solar Retinopathy: Etiology, Diagnosis, and Treatment. Retinal Physician, Volume 10, Issue: October 2013, pages 46-50.

2. Azar D, Stark W, Dodick J, et al. Prospective, randomized vector analysis of astigmatism after three-, one-, and no-suture phacoemulsification. J Cataract Refract Surg 1997; 23:1164-1173.

3. Conover, W.J. (1980). Practical Nonparametric Statistics 2 ed. J. Wiley, New York.