SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Femtosecond Laser System for refractive correction

Device Trade Name: VisuMax® Femtosecond Laser

Device Procode: OTL

Applicant's Name and Address: Carl Zeiss Meditec Inc.
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Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P150040

Date of FDA Notice of Approval: September 13, 2016

II. INDICATIONS FOR USE

The VisuMax® Femtosecond Laser is indicated for use in small incision lenticule extraction (SMILE) for the reduction or elimination of myopia ≥ -1.00 D to ≤ -8.00 D, with ≤ -0.50 D cylinder and MRSE ≤ -8.25 D in the eye to be treated in patients who are 22 years of age or older with documentation of stable manifest refraction over the past year as demonstrated by a change of ≤ 0.50 D MRSE.

III. CONTRAINDICATIONS

VisuMax SMILE procedure for the correction of myopia is contraindicated in patients with:

- a residual stromal bed thickness that is less than 250 microns from the corneal endothelium;
- abnormal corneal topographic findings, e.g., keratoconus, pellucid marginal degeneration;
- ophthalmoscopic signs of progressive or unstable myopia or keratoconus (or keratoconus suspect);
- irregular or unstable (distorted/not clear) corneal mires on central keratometry images;
- severe dry eye;
- active eye infection or inflammation;
- recent herpes eye infection or problems resulting from past infection;
- active autoimmune disease or connective tissue disease;

- uncontrolled diabetes;
- uncontrolled glaucoma.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the VisuMax® Femtosecond Laser labeling.

V. DEVICE DESCRIPTION

The VisuMax® Femtosecond Laser (Figure 1) is a precision ophthalmic surgical laser designed for the creation of incisions in the cornea. The action of the VisuMax and other femtosecond lasers mimics the cutting action of mechanical or blade-based keratomes. The VisuMax accomplishes this by scanning tightly focused patterns of femtosecond laser pulses in the cornea at precise and predefined positions and depths. Each laser pulse produces a micro-photodisruption in tissue of only a few microns in size. Patterns of contiguous, focused laser pulses results in the creation of continuous cut surfaces in the cornea.

Figure 1. VisuMax® Femtosecond Laser

Table 1. The VisuMax® Femtosecond Laser System consists of the following major components:

Laser Console	The Laser Console houses the femtosecond laser source, the scanning delivery system, the computer and software-hardware control system, an uninterruptible electrical power supply, the power supply distribution electronics, a visualization system and surgical microscope, two slit illumination units, the interface hardware for the Treatment Pack, user controls and user interface.
Patient Supporting	The Patient Supporting System (PSS) is used to support the patient in a supine position during corneal surgery with the VisuMax® Femtosecond Laser. The PSS

System	is also used to properly position the patient with respect to the Treatment Pack affixed to the treatment objective lens in the Laser Console. The joystick control on the PSS is manipulated by the user to position the patient with respect to the Treatment Pack, and to applanate and immobilize the eye of the patient in preparation for laser treatment.
Accessories - Treatment Pack	The VisuMax Treatment Pack is a pre-sterilized, single-use disposable accessory to the VisuMax® Femtosecond Laser. It consists of disposable elements that allow for the laser beam to be properly coupled onto a patient's cornea in a precise and controlled manner. No cleaning, disinfection or re-sterilization by the user is required or permitted. The Treatment Pack is contained in the blister pack that has been tested to maintain the sterility of the inner contents during the labeled shelf life using accepted international standards and accelerated test conditions accompanied by real life testing.

For the small incision lenticule extraction procedure, an intrastromal lenticule is created with the femtosecond laser in a shape corresponding to the desired refractive correction in the intact cornea. The femtosecond incisions for the SMILE procedure consist of four separate cuts (posterior cut, side cut for the lenticule, cap cut (anterior cut), and side cut for the opening incision), which are completed in succession in the procedure. The lenticule is subsequently accessed and removed by the surgeon through the opening incision.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative methods of correcting spherical myopia include: spectacle correction (glasses), contact lenses, photorefractive keratectomy (PRK), Laser-Assisted In Situ Keratomileusis (LASIK, including conventional LASIK, wavefront-guided LASIK, and topography-guided LASIK), and phakic intraocular lenses.

Each alternative has its own advantages and disadvantages. A prospective patient should fully discuss these alternatives with his/her eye care provider to select the method that is best for the patient.

VII. MARKETING HISTORY

The Carl Zeiss Meditec VisuMax® Femtosecond Laser, including the lenticule removal procedure, is commercially available in more than 200 countries, including the following: Algeria, Australia, Austria, Belgium, Brazil, Bulgaria, Canada, Czech Republic, China, Croatia, Denmark, Egypt, Estonia, Finland, France, Germany, Greece, Hong Kong, Hungary, India, Indonesia, Israel, Italy, Iceland, Ireland, Japan, Kazakhstan, Kuwait, Latvia, Liechtenstein, Lithuania, Luxembourg, Malaysia, Morocco, Mexico, Netherlands, New Zealand, Norway, Philippines, Poland, Portugal, Romania, Russia, Saudi Arabia, Singapore, Slovakia, Slovenia, South Africa, South Korea, Spain, Sweden, Switzerland, Taiwan, Thailand, Turkey, United Arab Emirates, United Kingdom, and Vietnam.

The Carl Zeiss Meditec VisuMax® Femtosecond Laser has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The potential adverse effects (e.g., complications) associated with the VisuMax SMILE procedure include, but are not limited to:

- Loss of BSCVA or contrast sensitivity;
- Over-correction or under-correction;
- Increase in refractive cylinder;
- Difficulty with night driving;
- Headache or eyestrain due to imbalance between the eyes;
- Worsening of patient complaints such as glare, halos, starbursts, hazy or blurred vision, distortion, double or ghost images, fluctuation of vision, focusing difficulty, difficulty with depth perception, light sensitivity; grittiness, and ocular pain/soreness;
- Transient light sensitivity syndrome;
- Dry eye;
- Ptosis;
- Increase in IOP;
- Lens opacity;
- Conjunctivitis;
- Iritis;
- Corneal haze/scar/infection/inflammation/infiltrate/ulcer/epithelial defect/epithelium in the interface/ edema/decompensation/striae or microstriae/ectasia;
- Perforated, miscreated, or melting of the cap;
- Treatment interruption, difficult lenticule removal with tissue damage or retained lenticule; ocular penetration;
- Retinal detachment/posterior vitreous detachment/vascular accidents.
- see in low-light conditions (e.g. reading a street sign at dusk)
- Unintentional imbalance between the two eyes causing headaches and eye strain

For the specific adverse events that occurred in the clinical study, please see Section X below.

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

i. Cut Shape Repeatability and Accuracy Testing

Testing was performed to confirm the repeatability of lenticule cut shapes and cut positions of the scanner in comparison to software-generated control signals. The shape and positioning of lenticule cuts produced by the VisuMax® Femtosecond Laser were examined by measuring lenticule cut surfaces in situ using laser scanning microscopy

(LSM). After a number of lenticule cuts were made in cutting ex vivo porcine corneas, LSM images of cross sections of cornea containing the lenticule cut surfaces were obtained and imaging software analysis was used to delineate the lenticule cut surfaces. The difference between the predicted thickness from the analytic model and the sampled measured thickness was used to determine the standard deviation (SD) in the differences. Similar procedures were used to determine SD for maximum thickness, lenticule diameter, and side cut angle. The results show that in all cases, the lenticule cut surface shapes and the lenticule cut positions met predefined acceptance criteria.
The in situ scanning and geometric parameters associated with the SMILE procedure were verified in studies conducted in porcine corneas. Testing was also performed to characterize the precision and repeatability of the geometric parameters in extracted lenticule. The test methods were similar for both studies. The primary parameters defining the extracted tissue geometry are the lenticule diameter and the lenticule thickness.
30 porcine eyes with a controlled IOP were treated using a range of settings. The lenticule thicknesses, cut surface curvatures, and cut positions were measured, and the deviations from predicted values were calculated. The tolerance for resection thickness was predefined to be ± 20 µm. The tolerance for both the upper and lower resection diameters was predefined to be ± 0.30 mm. Acceptance criteria were met for all parameter settings.
To further validate cut geometry, a second study treated 40 additional ex-vivo porcine eyes using a range of settings. Actual measurements were compared to predetermined parameter specifications. Four different resection thicknesses were performed in 10 eyes for each thickness, for a total of 40 eyes. The resection diameters were held constant across the four resection thicknesses. Lenticules were measured after extraction. For each set of data obtained at a particular predetermined intended central thickness, the mean deviation from the intended was calculated. The 95% confidence interval of the mean deviation from intended was then calculated. The mean deviation from the intended thickness, and the 95% confidence interval of the mean deviation from intended were very small, showing good consistency and reproducibility of the resection thickness.

ii. Cut Quality Testing

Environmental scanning electron microscope (eSEM) imaging was also performed on cadaver corneas to compare corneal cut quality of the VisuMax® Femtosecond Laser against the IntraLase FS femtosecond laser keratome. A total of 14 human globes (7 pairs) were cut with results establishing comparable outcomes to these accepted methods of corneal lamellar resections. Furthermore, an eSEM evaluation of the specific laser scanning parameters studied in IDE G110040 revealed well-defined, continuous cut edges with good lenticule surface quality for both posterior and anterior surfaces.

B. <u>Animal Studies</u>

Rabbit and porcine models were used to optimize the laser scanning parameters and to assess the safety of the lenticule removal procedure in preparation for clinical evaluation. Twenty-two White New Zealand rabbits (aged 20 weeks), and four domestic swine (aged 14 weeks) were used in total, and the study was divided into several phases. The initial phase focused on evaluating the potential of several diagnostic devices to characterize the animal eyes and to measure refractive changes.

In the second phase, laser scanning parameters were evaluated. Acute experiments (same day sacrifice) were conducted in 14 eyes, with a focus on optimizing the laser and scan parameters for best quality tissue cutting and dissection. Smaller separation distances combined with low pulse energies appeared to show less surface roughness than large spot distances with higher pulse energies. Based on these findings, a spot distance of 2 μm and pulse energy of 0.35 μJ were chosen as the parameters for the experiments characterizing refractive changes. Optimal parameters from this phase were used in the subsequent experiments in rabbits and pigs.

In a third phase, 15 live rabbits underwent actual lamellar resection and lenticule removal. A variety of corrections were attempted, ranging from -5 to +5 diopters sphere correction and from 0 to +5 diopters cylinder correction. These animals were followed for between 1 and 12 weeks. During the course of the refractive treatment evaluations, it was determined that rabbits are an inadequate model for the assessment of refractive corrections due to how thin and compliant rabbit corneas were.

In a final phase, both eyes of 4 pigs were treated with high pulse energies (i.e., exaggerated exposure). Histologic preparations were evaluated to assess retinal and ocular safety limits. Analysis of the fundus photographs and evaluation of the histological sections showed no alteration of the retina after laser treatment in either pig or rabbit models. The pigs were treated with pulse energies up to 2.5 times greater than the normally used pulse energy. In two pig eyes, the laser treatment was performed more than once using the higher pulse energy, with no injury to the retina. Slit lamp examination and histological sections showed no alterations of the crystalline lens. The laser therapy produced no side effects and appeared safe for use in the eye. Extraction of lenticules having the intended dimensions and prospective laser scanning parameters was successfully performed in the porcine and rabbit models.

C. Additional Studies

i. Electrical Safety, Electromagnetic Compatibility, and Laser Safety Testing

The VisuMax® Femtosecond Laser was tested by accredited third-party laboratories to ensure compliance with the applicable international standards for electromagnetic compatibility, electrical safety and laser safety. These standards include IEC 60601-1 3rd Edition 2005 C1:2006 + C2:2007 (General Requirements for Safety), IEC 60601-1-2 3rd Edition 2007 (Electromagnetic Compatibility Requirements and Tests), IEC 60601-1-4 3rd Edition 2007 (Programmable Electrical Medical Systems), IEC 60601-2-22 3rd Edition 2007 (Particular Requirements for the Safety of Diagnostic and Therapeutic Laser Equipment), IEC 60825-1 3rd Edition 2007 (Safety of Laser Products, Part 1 - Equipment Classification, and Requirements), and IEC 60825-5 3rd Edition 2007 (Safety of Laser Products – Manufacturer's Checklist). Additionally, the VisuMax® Femtosecond Laser meets all relevant design and performance standards for light-emitting products as defined in 21 CFR Part 1040.

ii. Software Validation Testing

Carl Zeiss Meditec procedures require the establishment and review of specifications, development of risk analysis, and adequate verifications and validation of software and hardware prior to release. Risk management procedures were applied according to current ISO 14791 and IEC 60601-1 standards.

Software testing was performed in accordance with IEC 60601-1-4 to verify and validate module and system level functions. The results of the overall validation testing demonstrate that the VisuMax® Femtosecond Laser meets all software specifications and requirements.

iii. VisuMax® Treatment Pack Testing

The VisuMax® Treatment Pack was cleared as part of K100253 and the following testing is incorporated by reference.

1. Biocompatibility

Biocompatibility testing was performed for the VisuMax® Treatment Pack according to ISO 10993-1.
The following materials of the VisuMax® Treatment Pack can contact the patient in normal use of the device according to its intended use: Contact lens, Glue, Contact Lens Holder.

Table 2. Biocompatibility testing on VisuMax® Treatment Pack

Test	Test Method	Test System	Results
Cytotoxicity	MEM Elution ISO 10993-5	L929 mammalian fibroblast cells	Non-cytotoxic
Sensitization	Maximization (NaCl and CSO extracts) ISO 10993-10	Guinea Pig	Non-sensitizer
Irritation	Intracutaneous (NaCl and CSO extracts) ISO 10993-10	Rabbits	Non-irritant

2. Sterility and Shelf Life Testing

The contents of the VisuMax® Treatment Pack (i.e., the Contact Lens, connecting hose, and filter) are provided sterile and are intended for single-use only. This accessory is the only component to the VisuMax provided sterile. No cleaning, disinfection or re-sterilization by the user is required or permitted. The treatment pack is sterilized by ethylene oxide to a Sterility Assurance Level (SAL) of 10^{-6}. The sterilization was validated in accordance to AAMI/ANSI/ISO 11135-1:2207 (Sterilization of health care products – Ethylene Oxide – Part 1).

The Treatment Pack is contained in the blister pack that has been tested to maintain the sterility of the inner contents during the labeled shelf life using accepted international standards and accelerated test conditions accompanied by real life testing. The shelf life has been determined at 2 years from the date of sterilization.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant initiated an investigational device exemption (IDE), US-based clinical study to establish a reasonable assurance of safety and effectiveness of the small incision lenticule extraction (SMILE) procedure using the VisuMax® Femtosecond Laser in subjects with myopia. Data from this clinical study were the bases for the PMA approval decision. A summary of the clinical study is presented below:

A. Study Design

Subjects were enrolled between July 9, 2012 and September 24, 2014. The database for this PMA reflected data collected through March 2, 2015 (database lock) and included 336 treated subjects. There are 5 investigational sites.

This is a prospective, multi-center, single-armed, unmasked clinical study. Subjects are to be followed for 12 months postoperatively.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the study was limited to subjects who met the following inclusion criteria:

1. Male and female subjects age 22 years of age and older;
2. Spherical myopia from ≥ -1.00 diopter (D) to ≤ -10.00 D, with ≤ -0.50 D cylinder and manifest refraction spherical equivalent (MRSE) ≤ -10.25 D, in the eye to be treated;
3. A stable refraction for the past year, as demonstrated by a change in MRSE of ≤ 0.50 D in the eye to be treated;
4. A difference between cycloplegic and manifest refractions of < 0.75 D spherical equivalent in the eye to be treated. (SE) is the difference between cycloplegic and manifest refractions;
5. Uncorrected visual acuity (UCVA) worse than 20/40 in the eye to be treated;
6. Best spectacle corrected visual acuity (BSCVA) at least 20/20 in the eye to be treated;
7. Discontinue use of contact lenses for at least 2 weeks (for hard lenses) or 3 days (for soft lenses) prior to the preoperative examination, and through the day of surgery; All contact lens wearers must demonstrate a stable refraction (within ±0.5 D), as determined by MRSE, on two consecutive examinations at least 1 week apart, in the eye to be treated;
8. Central corneal thickness of at least 500 microns in the eye to be treated;
9. Willing and able to return for scheduled follow-up examinations;

10. Able to provide written informed consent and follow study instructions in English.

Subjects were not permitted to enroll in the study if they met any of the following exclusion criteria:

1. Mesopic pupil diameter > 8.0 mm;
2. Cylinder greater than -0.50 D;
3. Treatment depth is less than 250 microns from the corneal endothelium;
4. Eye to be treated is targeted for monovision;
5. Fellow eye has BSCVA worse than 20/40;
6. Abnormal corneal topographic findings, e.g. keratoconus, pellucid marginal degeneration, in either eye;
7. History of or current anterior segment pathology, including cataracts in the eye to be treated;
8. Clinically significant dry eye syndrome unresolved by treatment in either eye;
9. Residual, recurrent, active ocular or uncontrolled eyelid disease, corneal scars or other corneal abnormality such as recurrent corneal erosion or severe basement membrane disease in the eye to be treated;
10. Ophthalmoscopic signs of progressive or unstable myopia or keratoconus (or keratoconus suspect) in either eye;
11. Irregular or unstable (distorted/not clear) corneal mires on central keratometry images in either eye;
12. History of ocular herpes zoster or herpes simplex keratitis;
13. Deep orbits, strong blink, anxiety, pterygium, or any other finding suggesting difficulty in achieving or maintaining suction;
14. Difficulty following directions or unable to fixate;
15. Previous intraocular or corneal surgery of any kind in the eye to be treated, including any type of surgery for either refractive or therapeutic purposes;
16. History of steroid-responsive rise in intraocular pressure, glaucoma, or preoperative intraocular pressure (IOP) > 21 mmHg in either eye;
17. History of diabetes, diagnosed autoimmune disease, connective tissue disease or clinically significant atopic syndrome;
18. Immunocompromised or requires chronic systemic corticosteroids or other immunosuppresive therapy that may affect wound healing;
19. History of known sensitivity to planned study medications;
20. Participating in any other ophthalmic drug or device clinical trial during the time of this clinical investigation;
21. Pregnant, lactating, or of child-bearing potential and not practicing a medically approved method of birth control.

2. Follow-up Schedule

All subjects who agreed to participate in the study were to return for follow-up examinations per the following schedule:

Patient Screening for Eligibility

Preoperative Evaluation: Day -60 to Day -1
Operative Evaluation: Day 0, day of surgery
Postoperative Day 1: Days 1
Postoperative Week 1: Days 5 to 9
Postoperative Month 1: Days 21 to 35 (Weeks 3 to 5)
Postoperative Month 3: Days 70 to 98 (Weeks 10 to 14)
Postoperative Month 6: Days 147 to 182 (Weeks 21 to 26)
Postoperative Month 9: Days 245 to 301 (Weeks 35 to 43)
Postoperative Month 12: Days 330 to 420 (Months 11 to 14)
Patient Exit.

The parameters to be measured preoperatively and postoperatively during the study are summarized in **Table 3** below.

Table 3. Visit Schedule:

Visits	Preop	Operative Visit	1 Day	7 Days	1 Month	3 Months	6 Months	9 Months	12 Months	Interim Visits[1]
UCVA	x		x	x	x	x	x	x	x	
BSCVA	x			x	x[1]	x[1]	x[1]	x[1]	x[1]	x[2,3]
Manifest refraction	x			x	x	x	x	x	x	x[3]
Cycloplegic refraction	x								x	
Computerized corneal topography	x					x	x	x	x	
Central keratometry	x					x	x	x	x	
Pupil size measurement (Mesopic)	x					x	x	x	x	
Wavefront Analysis	x					x			x	
Dilated fundus examination	x					x			x	
Pachymetry	x				x					
Slit lamp exam	x		x	x	x	x	x	x	x	x
Intraocular pressure	x				x	x	x	x	x	
Mesopic contrast sensitivity	x					x	x	x	x	
Subject Questionnaire	x					x	x	x	x	
Intraoperative events		x								
Adverse events		x	x	x	x	x	x	x	x	x

[1]Clinical assessments performed at interim visits are at the discretion of the investigator based on the patient's condition at presentation.

[2] If the visual acuity with spectacle correction is 2 or more lines below that obtained preoperatively, a rigid contact lens over refraction should be performed to estimate the best possible corrected visual acuity if deemed appropriate by the study investigator based on the subject's clinical presentation.

[3] For interim visits ≤ 7 days postoperative or any interim visit in which the subject presents with a condition that precludes performing a manifest refraction (e.g., central corneal abrasion), pinhole acuity will be obtained.

The patient reported outcomes (PRO) instrument ("subject questionnaire") used in IDE clinical study consisted of the Quality of Vision (QoV) questionnaire with accompanying photographs, and 2 of the 3 domains of the Ocular Surface Disease Index (OSDI). The modified QoV used in this trial could not be determined to be a reliable measure of visual symptoms by the FDA. Therefore, the reported prevalence and severity of symptoms may not be accurate. The study protocol specified that the PRO instrument was to be administered at the preoperative visit and at 3, 6, 9, and 12 months postoperatively. Study subjects self-administered the PRO instrument directly to reduce the potential for bias from an interviewer. The QoV instrument had three domains (frequency, severity, and bothersome) each consisting of 10 items that evaluate glare, halos, starbursts, hazy vision, blurred vision, distortion, double or multiple images, fluctuation of vision, focusing difficulties, and judging distance or depth perception. The two domains of the OSDI included all questions related to ocular symptoms and all questions related to environmental triggers.

Adverse events and complications were to be recorded at all visits.

The key postoperative time points were the point of refractive stability for the cohort (6 months) and the 12-month visit.

3. Clinical Endpoints
With regards to safety, the key outcomes for the study were:

1. Preservation of Best-Spectacle Corrected Visual Acuity (BSCVA)

a. In eyes with preoperative BSCVA 20/20 or better, percentage of eyes with BSCVA worse than 20/40 at the postoperative interval at which stability has been established.

b. Percentage of eyes with ≥ 2 lines BSCVA loss.

2. Induced Manifest Refractive Astigmatism

Percentage of eyes with induced cylinder of >2.00D at the postoperative interval at which stability has been established.

3. Loss of Contrast Sensitivity

a. Mean of "within-eye" loss of contrast sensitivity from baseline to 12 months with the 1-sided 95% confidence interval for each spatial frequency.

b. The percentage of eyes showing ≥ 0.3 log units loss at two or more spatial frequencies.

4. Incidence of Adverse Events

The counts and percentages of eyes for each adverse event.

Patient reported symptoms, stratified by pupil size and fellow eye status, are a secondary safety outcome.

Additional safety outcomes include corneal topography and wavefront aberrometry results.

With regard to effectiveness, the key outcomes for the study were:

1. **Predictability**: The percentage of eyes at the point at which stability is first achieved with MRSE:
   a. Within ± 1.00 D of the intended outcome.
   b. Within ± 0.50 D of the intended outcome.

2. **Improvement in uncorrected visual acuity (UCVA) Following Treatment**
   a. The percentage of eyes targeted for emmetropia that achieve UCVA of 20/40 or better at the postoperative interval at which stability has been established.
   b. Percentage of eyes targeted for emmetropia that achieve an UCVA of 20/20 or better.

Stability is considered to have been achieved at the latter of two postoperative refractions performed at least 3 months apart or at 3 months after surgery when compared with the 1-month interval, if at least three of the four following stability criteria are met:

1. At least 95% of the treated eyes should have a change ≤ 1.00 D of MRSE at the latter of two postoperative refractions performed at least 3 months apart or at 3 months after surgery when compared with the 1-month interval;
2. The mean rate of change in MRSE, as determined by paired analysis, is ≤ 0.5 D per year (0.04 D/month) over the same time period;
3. The mean rate of change of MRSE decreases monotonically over time, with a projected asymptote of zero or a rate of change attributable to normal aging;
4. The 95% confidence interval for the mean rate of change includes zero or a rate of change attributable to normal aging.

Stability is confirmed at least 3 months after the stability time point by a statistically adequate subgroup.

B. Accountability of PMA Cohort

At the time of database lock, of the 336 subjects who underwent surgery in the PMA study, 93 % (n=311) were available for analysis at the12-month visit. Accountability is summarized in **Table 4** below.

Table 4. Accountability: All Treated Eyes:

Enrolled (N = 336)	Day 1	Week 1	Month 1	Month 3	Month 6	Month 9	Month 12
Available for analysis	335 (99.7%)	334 (99.4%)	335 (99.7%)	333 (99.1%)	329 (97.9%)	320 (95.2%)	311 (92.6%)
Active	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	8 (2.4%)	17 (5.1%)
Missing	1 (0.3%)	2 (0.6%)	1 (0.3%)	3 (0.9%)	7 (2.1%)	8 (2.4%)	8 (2.4%)
Discontinued	1 (0.3%)	1 (0.3%)	1 (0.3%)	1 (0.3%)	2 (0.6%)	2 (0.6%)	3 (0.9%)
Death	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
Alternative treatment	1 (0.3%)	1 (0.3%)	1 (0.3%)	1 (0.3%)	2 (0.6%)	2 (0.6%)	2 (0.6%)
Scheduled visit data outstanding	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.3%)	2 (0.6%)	2 (0.6%)	0 (0.0%)
Lost to follow-up	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	3 (0.9%)	4 (1.2%)	5 (1.5%)
% Accountability	335 (100.0%)	334 (99.7%)	335 (100.0%)	333 (99.4%)	329 (98.5%)	320 (98.2%)	311 (98.4%)

% = n ÷ N x 100.

% Accountability = available ÷ (enrolled - discontinued - active) x 100

Of the 336 subjects that underwent surgery, three were excluded from the effectiveness population – two subjects who underwent alternative treatments and one subject who underwent treatment on the wrong eye. Out of the 333 subjects in the effectiveness cohort, 328 were available for analysis at the 6-month postoperative time point and 310 were available for analysis at the 12-month postoperative time point.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are summarized in **Table 5** below. The baseline preoperative refractive parameters are summarized in **Table 6** below.

Table 5. Demographics: All Treated Eyes:

Demographics	All Treated Eyes	
	Number	Percentage
NUMBER OF EYES & SUBJECTS	336 Eyes of 336 Subjects	
GENDER		
Male	140	41.7 %
Female	196	58.3 %
RACE		
White	309	92.0 %
Black	10	3.0 %
Asian	6	1.8 %
Other	11	3.3 %

SURGICAL EYE		
Right	152	45.2 %
Left	184	54.8 %
AGE (In Years)		
Mean (SD)	33.3 (7.9)	
Min., Max.	22.0, 58.0	
Fellow-eye Status		
Excimer Laser Refractive Surgery	333	99.1 %
Untreated	3	0.9 %

Table 6. Preoperative Refraction Parameters:

Manifest Refraction	All Treated Eyes		Effectiveness Population	
	Number	**%**	**Number**	**%**
Sphere				
0.00 to -1.00 D	4	1.2	4	1.2
-1.01 to -2.00 D	35	10.4	35	10.5
-2.01 to -3.00 D	54	16.1	53	15.9
-3.01 to -4.00 D	50	14.9	50	15.0
-4.01 to -5.00 D	50	14.9	49	14.7
-5.01 to -6.00 D	43	12.8	43	12.9
-6.01 to -7.00 D	44	13.1	44	13.2
-7.01 to -8.00 D	29	8.6	28	8.4
-8.01 to -9.00 D[1]	15	4.5	15	4.5
-9.01 D or higher[1]	12	3.6	12	3.6
Mean (SD)	*-4.762 (2.202)*		*-4.763 (2.202)*	
Range	*-10.00 to -1.00*		*-10.00 to -1.00*	
Total	336	100.0	333	100.0
Cylinder				
0.00 D	153	45.5	152	45.6
-0.25 D	105	31.3	105	31.5
-0.50 D	78	23.2	76	22.8
Mean (SD)	*-0.194 (0.200)*		*-0.193 (0.199)*	
Range	*-0.50 to 0.00*		*-0.50 to 0.00*	
Total	336	100.0	333	100.0

[1] Please note that treatment of these dioptric powers will present a flagged warning to the users so that the user understands that correction of these powers had not been substantiated by an adequate set of data.

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the full cohort of 336 subjects who underwent surgery. The key safety outcomes for this study are presented below in **Tables 7 to 8**. Adverse effects are reported in **Tables 9 to 10**. The secondary safety outcomes are presented below in **Tables 11 to 12**. Additional safety outcomes are presented below in **Tables 13 to 14**.

Table 7. Summary of Key Safety Variables at 6-Month Point of Refractive Stability
All Treated Eyes:

Key Safety Event	n/N	%	95 % CI[1]
Loss of ≥ 2 lines BSCVA	0/329	0.0 %	(0.0 %, 1.1 %)
BSCVA worse than 20/40 if 20/20 or better preoperatively	0/329	0.0 %	(0.0 %, 1.1 %)
Increased manifest refractive astigmatism > 2.0 D	0/329	0.0 %	(0.0 %, 1.1 %)

N = Number of case report forms (CRFs) received with non-missing values at each visit.
95 % CI was calculated based on Clopper-Pearson exact method.

Table 8. Log Contrast Sensitivity Change from Preoperative Visit All Treated Eyes:

Frequency	Statistics	Preop	Month 3	Month 6	Month 9	Month 12
A (1.5 cpd)	N	335	333	329	320	311
	Mean (SD)	1.584 (0.226)	1.606 (0.230)	1.658 (0.212)	1.653 (0.222)	1.665 (0.224)
	Q1, Q2, Q3	1.40, 1.56, 1.70	1.40, 1.56, 1.85	1.56, 1.70, 1.85	1.48, 1.56, 1.85	1.56, 1.70, 1.85
	Min., Max.	0.95, 2.00	0.85, 2.00	0.95, 2.00	0.95, 2.00	0.95, 2.00
	< 0.85	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Not Reported	1	0	0	0	0
B (3 cpd)	N	335	333	329	320	311
	Mean (SD)	1.800 (0.211)	1.839 (0.214)	1.882 (0.215)	1.886 (0.203)	1.907 (0.209)
	Q1, Q2, Q3	1.76, 1.76, 1.90	1.76, 1.90, 2.06	1.76, 1.90, 2.06	1.76, 1.90, 2.06	1.76, 1.90, 2.06
	Min., Max.	1.18, 2.20	1.00, 2.20	1.00, 2.20	1.00, 2.20	1.00, 2.20
	< 1.00	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Not Reported	1	0	0	0	0
C (6 cpd)	N	335	333	329	320	311
	Mean (SD)[1]	< 1.749 (> 0.240)	< 1.785 (> 0.254)	< 1.826 (> 0.252)	< 1.846 (> 0.245)	< 1.883 (> 0.250)
	Q1, Q2, Q3	1.52, 1.81, 1.95	1.65, 1.81, 1.95	1.65, 1.81, 2.11	1.65, 1.81, 2.11	1.65, 1.95, 2.11
	Min., Max.[1]	< 1.08, 2.26	< 1.08, 2.26	< 1.08, 2.26	< 1.08, 2.26	< 1.08, 2.26
	< 1.08	5 (1.5%)	4 (1.2%)	1 (0.3%)	3 (0.9%)	1 (0.3%)
	Not Reported	1	0	0	0	0
D (12 cpd)	N	335	333	329	320	311
	Mean (SD)[1]	< 1.349 (> 0.305)	< 1.353 (> 0.303)	< 1.408 (> 0.323)	< 1.424 (> 0.335)	< 1.469 (> 0.339)
	Q1, Q2, Q3	1.18, 1.34, 1.63	1.18, 1.34, 1.48	1.18, 1.48, 1.63	1.18, 1.48, 1.63	1.18, 1.48, 1.78
	Min., Max.[1]	< 0.90, 2.08	< 0.90, 2.08	< 0.90, 2.08	< 0.90, 2.08	< 0.90, 2.08
	< 0.90	24 (7.2%)	35 (10.5%)	27 (8.2%)	23 (7.2%)	22 (7.1%)
	Not Reported	1	0	0	0	0
0 patch at one or more cpds		24 (7.2%)	35 (10.5%)	27 (8.2%)	23 (7.2%)	22 (7.1%)

One subject had an alternative treatment after the 3-month visit and one subject had an alternative treatment at the operative visit.
Records after alternative treatment were excluded. Both were followed for safety after the alternative treatment. One subject had the incorrect eye treated. The treated OS did not have the contrast sensitivity test preoperatively.
N = Number of CRFs received with non-missing values at each visit. Not Reported = Number of CRFs received with missing values at each visit. Q1 = first quartile, Q2 = second quartile (median), and Q3 = third quartile.

[1] Number of subjects that could not read any patch at the respective spatial frequency. 0.85, 1.00, 1.08, and 0.90 are the lowest measurable contrast sensitivity values at 1.5, 3, 6, and 12 cpd, respectively. These lowest values were used for statistical calculation. In case of no patches could be read, a "<" sign was included in the Mean and Minimum, and ">" sign was included in the SD.

Adverse effects that occurred in the PMA clinical study:

Table 9. Intraoperative Adverse Events:

Intraoperative AE	n
Difficult lenticule removal with tissue Damage	2 (0.6%)
Perforated cap	1 (0.3%)
Retained tissue, small	1 (0.3%)

Table 10. Additional Intraoperative Events All Treated Eyes:

N = 336	Number	Percent
Difficult lenticule removal without tissue damage	8	2.4 %
Loss of suction: completed treatment	4	1.2 %
Loss of suction: discontinued treatment	2	0.6 %
Decentered treatment*	1	0.3%
Any Events	15	4.5 %

Multiple events could be reported for each subject.
Percent = Number/N ×100.
* Identified by postoperative topography

Table 11. Postoperative Ophthalmic Adverse Events — All Treated Eyes:

AE	D1 N=335	W1 N=334	M1 N=335	M3 N=333	M6 N=329	M9 N=320	M12 N=311	Uns N=24	Cum N=336
Diffuse lamellar keratitis (Stage 3 or above)	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
Corneal infiltrate or ulcer	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
Any persistent corneal epithelial defect at 1 month or later	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
Corneal edema at 1 month or later	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
Epithelium in the interface with loss of 2 lines (10 letters) or more of BSCVA	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
Melting of the cap	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
IOP increase of > 10 mmHg above baseline or IOP > 30 mmHg on 2 consecutive exams	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
Haze beyond 6 months with loss of 2 lines or greater (≥10 letters) of BSCVA	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
Decrease in BSCVA of greater than or equal to 2 lines (≥10 letters) not due to irregular astigmatism as shown by hard contact lens refraction at 3 months or later	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1	1 0.3%
Retinal Detachment	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
Retinal vascular accidents	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%
Ocular penetration	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0	0 0.0%

Any other vision-threatening event									
Retinal vasculitis	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1 0.3%	0	1 0.3%
Other									
Carcinoma in situ, conjunctival	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1 0.3%	0	1 0.3%
Conjunctivitis, allergic	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1 0.3%	0 0.0%	0	1 0.3%
Conjunctivitis, viral	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1	1 0.3%
Herpetic lid and corneal lesion	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1	1 0.3%
Iritis	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1	1 0.3%
PVD	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1 0.3%	0 0.0%	0	1 0.3%
Pyogenic Granuloma	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1 0.3%	0 0.0%	0 0.0%	1	1 0.3%
Retained tissue, small	2 0.6%	2 0.6%	1 0.3%	1 0.3%	0 0.0%	0 0.0%	0 0.0%	1	2* 0.6%

Multiple events could be reported for each subject.

Uns = interim visit, N is the number of eyes with interim visits, and incidence is the number of eyes with the reported events during the interim visits.

Cum = cumulative, N is the number of all treated eyes with postoperative visits, and incidence is the number of eyes with the reported events during the study.

*One of these subjects is also accounted for in Table 7, as the retained tissue was first observed intraoperatively.

Through the point of data lock, a total of 14 subjects were reported with 15 ocular adverse events (AEs) over the course of the study. Four intraoperative events were reported as AEs. Ten subjects experienced adverse events postoperatively.

Table 12. Complications All Treated Eyes:

Complications	**D0 N=336**	**D1 N=335**	**W1 N=334**	**M1 N=335**	**M3 N=333**	**M6 N=329**	**M9 N=320**	**M12 N=311**	**Uns N=24**	**Cum N=336**
Clinical signs and/or subject symptoms consistent with dry eye	0 0.0 %	0 0.0 %	5 1.5 %	1 0.3 %	4 1.2 %	0 0.0 %	0 0.0 %	0 0.0 %	3	9 2.7 %
Corneal edema between 1 week and 1 month after procedure	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0	0 0.0 %
Corneal scarring	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0	0 0.0 %
Crystalline lens opacity	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0	0 0.0 %
Diffuse lamellar keratitis (Stage 2 or less)	0 0.0 %	1 0.3 %	3 0.9 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0	3 0.9 %
Epithelium in the interface	0 0.0 %	1 0.3 %	2 0.6 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0	3 0.9 %
Foreign body sensation at 1 month or later	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	1 0.3 %	1 0.3 %	0 0.0 %	0	1 0.3 %
Ghost/double images in the operative eye	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0	0 0.0 %
Interface debris, such as lint, pigment, air bubbles, and meibomian gland secretions	0 0.0 %	5 1.5 %	5 1.5 %	2 0.6 %	2 0.6 %	0 0.0 %	0 0.0 %	0 0.0 %	1	9 2.7 %
Moderate or severe glare	0 0.0 %	0 0.0 %	0 0.0 %	1 0.3 %	21 6.3 %	15 4.6 %	7 2.2 %	4 1.3 %	0	35 10.4 %
Moderate or severe halos	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	10 3.0 %	11 3.3 %	4 1.3 %	1 0.3 %	0	20 6.0 %

Pain at 1 month or later	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	1 0.3 %	1 0.3 %	1 0.3 %	1 0.3 %	0	1 0.3 %
Striae/microstriae	0 0.0 %	0 0.0 %	0 0.0 %	1 0.3 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0	1 0.3 %
Transient light sensitivity syndrome (TLSS)	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	1	1 0.3 %

Multiple events could be reported for each subject.

Uns = interim visit, N is the number of eyes with interim visits, and incidence is the number of eyes with the reported events during the interim visits.

Cum = cumulative, N is the number of all treated eyes with postoperative visits, and incidence is the number of eyes with the reported events during the study. One subject did not complete VisuMax treatment and had an alternative treatment at the operative visit. Since the data after the alternative treatment were not included, the total number of subjects with postoperative visits was 335.

Three secondary interventions for epithelial ingrowth or interface debris were performed at or before the 1-week time point, one involving an irrigation to remove interface debris and two involving irrigation with Balanced Salt Solution (BSS) to remove epithelial cells in the interface.

Secondary Safety Outcomes: Patient Reported Symptoms

The PRO instrument ("subject questionnaire" or questionnaire) used in IDE clinical study consisted of the QoV questionnaire with accompanying photographs, and 2 of the 3 domains of the OSDI. The modified QoV used in this trial could not be determined to be a reliable measure of visual symptoms by the FDA. Therefore, the reported prevalence and severity of symptoms may not be accurate. The study protocol specified that the PRO instrument was to be administered at the preoperative visit and at 3, 6, 9, and 12 months postoperatively. Study subjects self-administered the PRO instrument directly to reduce the potential for bias from an interviewer. The QoV instrument had three domains (frequency, severity, and bothersome) each consisting of 10 items which evaluate glare, halos, starbursts, hazy vision, blurred vision, distortion, double or multiple images, fluctuation of vision, focusing difficulties, and judging distance or depth perception. The two domains of the OSDI included all questions related to ocular symptoms and all questions related to environmental triggers.

Results from the questionnaire are summarized in **Tables 13 and 14** below.

Table 13. Frequency of Moderate and Severe Dry Eye Symptoms Classified by OSDI Scores All Treated Eyes:

Severity of Dry Eye Symptoms	Preop	Month 6	Month 12	Last Available Visit
N	335	329	309	336
Moderate	16 (5%)	21 (6%)	7 (2%)	10 (3%)
Severe	10 (3%)	6 (2%)	8 (3%)	9 (3%)
Not Reported	1	0	2	0

OSDI score = (sum of scores) x 25/ (# of questions answered). The responses of N/A were excluded.

"Moderate": OSDI score ≥ 23 to < 33. "Severe": OSDI score ≥ 33.

Scoring based on Miller et al. Minimal Clinically Important Difference for the Ocular Surface Disease Index *Arch Ophthalmol.* 2010;128(1):94-101.

Table 14. Two Highest Categories of Bothersome and Severity for Each QoV Symptom at 12 Months:

Visual Symptom	Number of patients out of 310 Total			
	Bothersome		Severity	
Glare	Quite	3 (1.0%)	Moderate	4 (1.3%)
	Very	0 (0.0%)	Severe	0 (0.0%)
	Total	3 (1.0%)	**Total**	4 (1.3%)
Halos	Quite	1 (0.3%)	Moderate	1 (0.3%)
	Very	0 (0.0%)	Severe	0 (0.0%)
	Total	1 (0.3%)	**Total**	1 (0.3%)
Starbursts	Quite	6 (1.9%)	Moderate	6 (1.9%)
	Very	0 (0.0%)	Severe	0 (0.0%)
	Total	6 (1.9%)	**Total**	6 (1.9%)
Hazy vision	Quite	0 (0.0%)	Moderate	0 (0.0%)
	Very	0 (0.0%)	Severe	0 (0.0%)
	Total	0 (0.0%)	**Total**	0 (0.0%)
Blurred vision	Quite	4 (1.3%)	Moderate	4 (1.3%)
	Very	0 (0.0%)	Severe	0 (0.0%)
	Total	4 (1.3%)	**Total**	4 (1.3%)
Distortion	Quite	0 (0.0%)	Moderate	0 (0.0%)
	Very	0 (0.0%)	Severe	0 (0.0%)
	Total	0 (0.0%)	**Total**	0 (0.0%)
Double or Multiple Images	Quite	2 (0.6%)	Moderate	3 (1.0%)
	Very	1 (0.3%)	Severe	1 (0.3%)
	Total	3 (1.0%)	**Total**	4 (1.3%)
Fluctuation	Quite	1 (0.3%)	Moderate	1 (0.3%)
	Very	0 (0.0%)	Severe	0 (0.0%)
	Total	1 (0.3%)	**Total**	1 (0.3%)
Focusing	Quite	3 (1.0%)	Moderate	2 (0.6%)
	Very	0 (0.0%)	Severe	1 (0.3%)
	Total	3 (1.0%)	**Total**	3 (1.0%)
Judging Distance or Depth Perception	Quite	5 (1.6%)	Moderate	2 (0.6%)
	Very	0 (0.0%)	Severe	0 (0.0%)
	Total	5 (1.6%)	**Total**	2 (0.6%)

Additional Safety Outcomes and Analyses:

Table 15. Topography Findings All Treated Eyes:

	Preop n/N (%)	**Month 3 n/N (%)**	**Month 6 n/N (%)**	**Month 9 n/N (%)**	**Month 12 n/N (%)**
Evaluable	335	332	325	319	311
Irregular Astigmatism	0/335 (0.0%)	0/332 (0.0%)	0/325 (0.0%)	0/319 (0.0%)	0/311 (0.0%)
Ectasia	0/335 (0.0%)	0/332 (0.0%)	0/325 (0.0%)	0/319 (0.0%)	0/311 (0.0%)
Tear Film Artifacts	3/335 (0.9%)	3/332 (0.9%)	9/325 (2.8%)	3/319 (0.9%)	5/311 (1.6%)
Decentration	NA	1/332 (0.3%)	2/325 (0.6%)	2/319 (0.6%)	2/311 (0.6%)
Other	0/335 (0.0%)	0/332 (0.0%)	0/325 (0.0%)	0/319 (0.0%)	0/311 (0.0%)
Topography not performed	1	1	4	1	0
Total	336	333	329	320	311

N = Number of eyes with non-missing values at each visit. % = n/N ×100.

There were seven reports of decentration greater than 1 mm, involving three subjects, but only one subject showed consistent decentration at all four scheduled postoperative visits indicating true decentration.

Table 16. Change in Wavefront Aberrometry from Preoperative Stratified by Largest Scan Size (mm) Treated Eyes with Preoperative, 3-Month, and 12-Month Visits:

Scan Size	Parameters	Statistics	Month 3	Month 12
4.0	**Change in Wavefront from Preoperative (micron)**			
	Total Higher Order RMS	N	106	106
		Mean (SD)	-0.001 (0.086)	-0.002 (0.079)
		Min, Max	-0.310, 0.234	-0.341, 0.142
	Coma	Mean (SD)	0.010 (0.087)	0.013 (0.079)
		Min, Max	-0.268, 0.258	-0.274, 0.199
	Spherical	Mean (SD)	-0.002 (0.047)	-0.002 (0.047)
		Min, Max	-0.201, 0.120	-0.180, 0.112
5.0	**Change in Wavefront from Preoperative (micron)**			
	Total Higher Order RMS	N	128	128
		Mean (SD)	0.049 (0.141)	0.051 (0.149)
		Min, Max	-0.293, 0.397	-0.311, 0.365
	Coma	Mean (SD)	0.070 (0.170)	0.064 (0.170)
		Min, Max	-0.288, 0.515	-0.420, 0.467
	Spherical	Mean (SD)	0.048 (0.100)	0.046 (0.101)
		Min, Max	-0.184, 0.400	-0.174, 0.339
6.0	**Change in Wavefront from Preoperative (micron)**			
	Total Higher Order RMS	N	16	16
		Mean (SD)	0.220 (0.268)	0.248 (0.314)
		Min, Max	-0.239, 0.766	-0.248, 0.806
	Coma	Mean (SD)	0.232 (0.289)	0.261 (0.326)
		Min, Max	-0.255, 0.793	-0.392, 0.874
	Spherical	Mean (SD)	0.129 (0.196)	0.149 (0.173)
		Min, Max	-0.285, 0.511	-0.255, 0.414
Overall	**Change in Wavefront from Preoperative (micron)**			
	Total Higher Order RMS	N	250	250
		Mean (SD)	0.039 (0.143)	0.041 (0.153)
		Min, Max	-0.310, 0.766	-0.341, 0.806
	Coma	Mean (SD)	0.055 (0.161)	0.055 (0.165)
		Min, Max	-0.288, 0.793	-0.420, 0.874
	Spherical	Mean (SD)	0.032 (0.098)	0.032 (0.097)
		Min, Max	-0.285, 0.511	-0.255, 0.414

N = Number of CRFs received with non-missing values at each visit.
The largest scan size was 4.0, 5.0, or 6.0 mm, depending on the largest scan size obtained at all the preoperative and postoperative visits

Table 17. Summary of Key Safety Variables at Last Available Visit All Treated Eyes:

Key Safety Event	n/N	%	95 % CI[1]
Loss of ≥ 2 lines BSCVA	0/336	0.0 %	(0.0 %, 1.1 %)
BSCVA worse than 20/40 if 20/20 or better preoperatively	0/336	0.0 %	(0.0 %, 1.1 %)
Increased manifest refractive astigmatism > 2.0 D	0/336	0.0 %	(0.0 %, 1.1 %)

N = Number of CRFs received with non-missing values at each visit.
95 % CI was calculated based on Clopper-Pearson exact method.

Table 18. Change in Best Spectacle-Corrected Visual Acuity (BSCVA) from Preop All Treated Eyes:

BSCV	Week 1 n	Week 1 (%)	Month 1 n	Month 1 (%)	Month 3 n	Month 3 (%)	Month 6 n	Month 6 (%)	Month 9 n	Month 9 (%)	Month 12 n	Month 12 (%)
Available (N)	334		335		333		329		319		311	
Lost > 2 lines (>10 letters)	13	(3.9 %)	5	(1.5 %)	0	(0.0 %)	0	(0.0 %)	0	(0.0 %)	0	(0.0 %)
Lost 2 lines (10 letters)	6	(1.8 %)	0	(0.0 %)	0	(0.0 %)	0	(0.0 %)	0	(0.0 %)	0	(0.0 %)
Lost 1 line (5-9 letters)	75	(22.5 %)	36	(10.7 %)	21	(6.3 %)	11	(3.3 %)	10	(3.1 %)	8	(2.6 %)
Unchanged (< 5 letters)	222	(66.5 %)	255	(76.1 %)	246	(73.9 %)	243	(73.9 %)	239	(74.9 %)	224	(72.0 %)
Gained 1 line (5-9 letters)	15	(4.5 %)	38	(11.3 %)	59	(17.7 %)	66	(20.1 %)	64	(20.1 %)	71	(22.8 %)
Gained 2 lines (10 letters)	0	(0.0 %)	1	(0.3 %)	4	(1.2 %)	6	(1.8 %)	3	(0.9 %)	3	(1.0 %)
Gained > 2 lines (>10 letters)	3	(0.9 %)	0	(0.0 %)	3	(0.9 %)	3	(0.9 %)	3	(0.9 %)	5	(1.6 %)
Not reported	0		0		0		0		1		0	
Total	334		335		333		329		320		311	

N = Number of CRFs received with non-missing values at each visit. % = (n/N) x 100

Table 19. QoV Score Change from Preoperative All Treated Eyes:

Sub-scale		Month 3	Month 6	Month 9	Month 12
Frequency	**N**	**332**	**328**	**319**	**309**
	Worse	176/332 (53%)	150/328 (46%)	133/319 (42%)	116/309 (38%)
	Same	70/332 (21%)	74/328 (23%)	74/319 (23%)	71/309 (23%)
	Improved	86/332 (26%)	104/328 (32%)	112/319 (35%)	122/309 (39%)
	Not Reported	1	1	1	2
Severity	**N**	**332**	**328**	**319**	**309**
	Worse	160/332 (48%)	131/328 (40%)	108/319 (34%)	93/309 (30%)
	Same	81/332 (24%)	97/328 (30%)	93/319 (29%)	95/309 (31%)
	Improved	91/332 (27%)	100/328 (30%)	118/319 (37%)	121/309 (39%)
	Not Reported	1	1	1	2
Bothersome	**N**	**332**	**328**	**319**	**309**
	Worse	138/332 (42%)	106/328 (32%)	95/319 (30%)	79/309 (26%)
	Same	102/332 (31%)	123/328 (38%)	119/319 (37%)	119/309 (39%)
	Improved	92/332 (28%)	99/328 (30%)	105/319 (33%)	111/309 (36%)
	Not Reported	1	1	1	2

Change = Postop - Preop (pairwise).
Worse: Change > 0. Same: Change = 0. Improved: Change < 0. Not Reported = Number of eyes with missing values at each visit.
% = (n/N) x 100

Table 20. Changes of 2 or More Grades in QoV Symptoms at 12 Months:

Symptom	Outcomes	Better n/N (%)	Worse n/N (%)
Glare	Frequency	5/309 (1.6%)	3/309 (1.0%)
	Severity	11/309 (3.6%)	3/309 (1.0%)
	Bothersome	7/309 (2.3%)	2/309 (0.6%)
	# of Subjects	17/309 (5.5%)	7/309 (2.3%)
Halos	Frequency	7/309 (2.3%)	4/309 (1.3%)
	Severity	4/309 (1.3%)	0/309 (0.0%)
	Bothersome	2/309 (0.6%)	0/309 (0.0%)
	# of Subjects	8/309 (2.6%)	4/309 (1.3%)
Starbursts	Frequency	1/309 (0.3%)	5/309 (1.6%)
	Severity	2/309 (0.6%)	3/309 (1.0%)
	Bothersome	0/309 (0.0%)	4/309 (1.3%)
	# of Subjects	3/309 (1.0%)	7/309 (2.3%)
Hazy Vision	Frequency	4/309 (1.3%)	1/309 (0.3%)
	Severity	2/309 (0.6%)	0/309 (0.0%)
	Bothersome	2/309 (0.6%)	0/309 (0.0%)
	# of Subjects	5/309 (1.6%)	1/309 (0.3%)
Blurred Vision	Frequency	3/309 (1.0%)	8/309 (2.6%)
	Severity	4/309 (1.3%)	4/309 (1.3%)
	Bothersome	5/309 (1.6%)	4/309 (1.3%)
	# of Subjects	5/309 (1.6%)	8/309 (2.6%)
Distortion	Frequency	1/309 (0.3%)	0/309 (0.0%)
	Severity	0/309 (0.0%)	0/309 (0.0%)
	Bothersome	1/309 (0.3%)	0/309 (0.0%)
	# of Subjects	1/309 (0.3%)	0/309 (0.0%)
Double or Multiple Images	Frequency	0/309 (0.0%)	4/309 (1.3%)
	Severity	0/309 (0.0%)	4/309 (1.3%)
	Bothersome	0/309 (0.0%)	3/309 (1.0%)
	# of Subjects	0/309 (0.0%)	5/309 (1.6%)
Fluctuation	Frequency	0/309 (0.0%)	2/309 (0.6%)
	Severity	2/309 (0.6%)	1/309 (0.3%)
	Bothersome	1/309 (0.3%)	1/309 (0.3%)
	# of Subjects	2/309 (0.6%)	2/309 (0.6%)
Focusing	Frequency	0/309 (0.0%)	2/309 (0.6%)
	Severity	7/309 (2.3%)	2/309 (0.6%)
	Bothersome	5/309 (1.6%)	2/309 (0.6%)
	# of Subjects	11/309 (3.6%)	3/309 (1.0%)
Judging Distance or Depth Perception	Frequency	6/309 (1.9%)	0/309 (0.0%)
	Severity	5/309 (1.6%)	1/309 (0.3%)
	Bothersome	4/309 (1.3%)	4/309 (1.3%)
	# of Subjects	9/309 (2.9%)	4/309 (1.3%)
	# of Subjects	39/309 (12.6%)	27/309 (8.7%)

N = Number of eyes with non-missing values the 12-Month visit. % = (n/N) ×100.
The symptoms with the two highest rates of 2-grades of worsening or more within each subscale are shaded.

Table 21. OSDI Score Change from Preoperative All Treated Eyes:

Sub-scale		Month 3	Month 6	Month 9	Month 12
Experienced Symptoms during the Last Week	**N**	**332**	**328**	**319**	**308**
	Worse	128/332 (39%)	92/328 (28%)	76/319 (24%)	73/308 (24%)
	Same	130/332 (39%)	145/328 (44%)	151/319 (47%)	144/308 (47%)
	Improved	74/332 (22%)	91/328 (28%)	92/319 (29%)	91/308 (30%)
	NA	0	0	0	0
	Not Reported	1	1	1	3
Felt Uncomfortable in Situations during the Last Week	**N**	**310**	**307**	**300**	**288**
	Worse	134/310 (43%)	119/307 (39%)	88/300 (29%)	87/288 (30%)
	Same	121/310 (39%)	127/307 (41%)	144/300 (48%)	138/288 (48%)
	Improved	55/310 (18%)	61/307 (20%)	68/300 (23%)	63/288 (22%)
	NA	22	21	19	20
	Not Reported	1	1	1	3

Change = Postop - Preop (pairwise).
Worse: Change > 0. Same: Change = 0. Improved: Change < 0.
NA = Number of subjects with "Not applicable" response to all questions of the sub-scale. The NA responses were not included in the OSDI score calculation. Subjects with NA to all questions of the sub-scale were excluded from the analyses.
Not Reported = Number of eyes with missing values at each visit.
% = (n/N) x 100

2. Effectiveness Results

The analysis of effectiveness was based on the 328 evaluable effectiveness cohort subjects at the stability (6-month) time point. Preoperatively, there were no eyes with UCVA of 20/40 or better. Key effectiveness outcomes are presented in **Table 22**. Analysis of stability is presented in **Table 23** below.

Table 22. Summary of Key Effectiveness Variables Effectiveness Cohort Eyes (key outcomes highlighted with grey background):

Key Effectiveness Variables	Week 1 n/N (%) 95 % CI	Month 1 n/N (%) 95 % CI	Month 3 n/N (%) 95 % CI	Month 6 n/N (%) 95 % CI	Month 9 n/N (%) 95 % CI	Month 12 n/N (%) 95 % CI
Effectiveness Variables (Effectiveness Population)						
UCVA, 20/16 or better	95/332 (28.6 %)	155/333 (46.5 %) (41.1 %, 52.1 %)	192/331 (58.0 %) (52.5 %, 63.4 %)	197/328 (60.1 %) (54.5 %, 65.4 %)	196/319 (61.4 %) (55.9 %, 66.8 %)	198/310 (63.9 %) (58.2 %, 69.2 %)
UCVA, 20/20 or better	210/332 (63.3 %)	262/333 (78.7 %) (73.9 %, 83.0 %)	282/331 (85.2 %) (80.9 %, 88.8 %)	287/328 (87.5 %) (83.4 %, 90.9 %)	281/319 (88.1 %) (84.0 %, 91.4 %)	273/310 (88.1 %) (83.9 %, 91.5 %)
UCVA, 20/25 or better	286/332 (86.1 %)	308/333 (92.5 %) (89.1 %, 95.1 %)	317/331 (95.8 %) (93.0 %, 97.7 %)	313/328 (95.4 %) (92.6 %, 97.4 %)	309/319 (96.9 %) (94.3 %, 98.5 %)	301/310 (97.1 %) (94.6 %, 98.7 %)
UCVA, 20/32 or better	315/332 (94.9 %)	324/333 (97.3 %) (94.9 %, 98.8 %)	324/331 (97.9 %) (95.7 %, 99.1 %)	322/328 (98.2 %) (96.1 %, 99.3 %)	315/319 (98.7 %) (96.8 %, 99.7 %)	305/310 (98.4 %) (96.3 %, 99.5 %)
UCVA, 20/40 or better	325/332 (97.9 %)	333/333 (100.0 %) (98.9 %, 100.0 %)	329/331 (99.4 %) (97.8 %, 99.9 %)	327/328 (99.7 %) (98.3 %, 100.0 %)	318/319 (99.7 %) (98.3 %, 100.0 %)	309/310 (99.7 %) (98.2 %, 100.0 %)
MRSE, Attempted vs. Achieved, ±0.25D	262/331 (79.2 %) (74.4 %, 83.4 %)	264/333 (79.3 %) (74.5 %, 83.5 %)	262/331 (79.2 %) (74.4 %, 83.4 %)	261/328 (79.6 %) (74.8 %, 83.8 %)	258/319 (80.9 %) (76.1 %, 85.0 %)	250/310 (80.6 %) (75.8 %, 84.9 %)
MRSE, Attempted vs. Achieved, ±0.50D	308/331 (93.1 %) (89.8 %, 95.5 %)	310/333 (93.1 %) (89.8 %, 95.6 %)	304/331 (91.8 %) (88.4 %, 94.6 %)	305/328 (93.0 %) (89.7 %, 95.5 %)	303/319 (95.0 %) (92.0 %, 97.1 %)	291/310 (93.9 %) (90.6 %, 96.3 %)

MRSE, Attempted vs. Achieved, ±1.00D	328/331 (99.1 %) (97.4 %, 99.8 %)	331/333 (99.4 %) (97.8 %, 99.9 %)	328/331 (99.1 %) (97.4 %, 99.8 %)	323/328 (98.5 %) (96.5 %, 99.5 %)	316/319 (99.1 %) (97.3 %, 99.8 %)	306/310 (98.7 %) (96.7 %, 99.6 %)
MRSE, Attempted vs. Achieved, ±2.00D	331/331 (100.0 %) (98.9 %, 100.0	333/333 (100.0 %) (98.9 %, 100.0 %)	331/331 (100.0 %) (98.9 %, 100.0 %)	328/328 (100.0 %) (98.9 %, 100.0 %)	319/319 (100.0 %) (98.9 %, 100.0 %)	310/310 (100.0 %) (98.8 %, 100.0 %)

N = Number of CRFs received with non-missing values at each visit.
95 % CI was calculated based on Clopper-Pearson exact method.

Stability:

Table 23. Stability of Manifest Refraction Spherical Equivalent (MRSE) Effectiveness Population:

Change in MRSE	Between 1 and 3 Months	Between 3 and 6 Months	Between 6 and 9 Months	Between 9 and 12 Months
Pairwise Sequential Visits				
Eyes within 0.50 D change (n/N, %, [% CI][1])	319/331 (96.4%) (93.8%, 98.1%)	317/327 (96.9%) (94.4%, 98.5%)	311/317 (98.1%) (95.9%, 99.3%)	301/308 (97.7%) (95.4%, 99.1%)
Eyes within 1.00 D change (n/N, %, [% CI][1])	331/331 (100.0%) (98.9%, 100.0%)	327/327 (100.0%) (98.9%, 100.0%)	316/317 (99.7%) (98.3%, 100.0%)	307/308 (99.7%) (98.2%, 100.0%)
Mean change between visits (D) SD 95% CI	-0.008 0.241 (-0.034, 0.018)	0.021 0.232 (-0.005, 0.046)	0.013 0.213 (-0.011, 0.037)	0.005 0.198 (-0.017, 0.027)
Mean change per month (D)	-0.004	0.007	0.004	0.002
Mean change per year (D) (change per month × 12)	-0.048	0.083	0.052	0.019
12-Month Consistent Cohort				
Eyes within 0.50 D change (n/N, %, [% CI][1])	296/305 (97.0%) (94.5%, 98.6%)	298/305 (97.7%) (95.3%, 99.1%)	301/305 (98.7%) (96.7%, 99.6%)	298/305 (97.7%) (95.3%, 99.1%)
Eyes within 1.00 D change (n/N, %, [% CI][1])	305/305 (100.0%) (98.8%, 100.0%)	305/305 (100.0%) (98.8%, 100.0%)	304/305 (99.7%) (98.2%, 100.0%)	304/305 (99.7%) (98.2%, 100.0%)
Mean change between visits (D) SD 95% CI	0.002 0.231 (-0.024, 0.028)	0.014 0.219 (-0.011, 0.039)	0.013 0.205 (-0.010, 0.036)	0.005 0.198 (-0.018, 0.027)
Mean change per month (D)	0.001	0.005	0.004	0.002
Mean change per year (D) (change per month × 12)	0.010	0.056	0.051	0.018

Pairwise Sequential Visits = Eyes that had two consecutive exams, but not necessarily every follow-up exam.
Consistent Cohort = All eyes examined at 1, 3, 6, 9 and 12 months.

1 95% CI was calculated based on Clopper-Pearson method.

Additional Effectiveness Analyses:

The results of key effectiveness variables were stratified by pre-operative manifest spherical equivalent (MRSPH) as shown in **Table 24** below.

Table 24. Summary of Key Effectiveness Variables at 6 Months Stratified By Preoperative MRSPH Effectiveness Population:

Key Effectiveness Variables	Preop MRSPH					
	0.00 to -1.00 D n/N (%)	-1.01 to -2.00 D n/N (%)	-2.01 to -3.00 D n/N (%)	-3.01 to -4.00 D n/N (%)	-4.01 to -5.00 D n/N (%)	-5.01 to -6.00 D n/N (%)
UCVA, 20/16 or better	2/4 (50.0%)	20/35 (57.1%)	35/52 (67.3%)	37/50 (74.0%)	32/48 (66.7%)	23/42 (54.8%)
UCVA, 20/20 or better	3/4 (75.0%)	32/35 (91.4%)	48/52 (92.3%)	48/50 (96.0%)	44/48 (91.7%)	35/42 (83.3%)
UCVA, 20/25 or better	4/4 (100.0%)	33/35 (94.3%)	51/52 (98.1%)	48/50 (96.0%)	47/48 (97.9%)	40/42 (95.2%)
UCVA, 20/32 or better	4/4 (100.0%)	35/35 (100.0%)	51/52 (98.1%)	48/50 (96.0%)	48/48 (100.0%)	40/42 (95.2%)
UCVA, 20/40 or better	4/4 (100.0%)	35/35 (100.0%)	52/52 (100.0%)	49/50 (98.0%)	48/48 (100.0%)	42/42 (100.0%)
MRSE, Attempted vs. Achieved, ±0.25D	3/4 (75.0%)	29/35 (82.9%)	45/52 (86.5%)	46/50 (92.0%)	40/48 (83.3%)	34/42 (81.0%)
MRSE, Attempted vs. Achieved, ±0.50D	4/4 (100.0%)	34/35 (97.1%)	50/52 (96.2%)	48/50 (96.0%)	45/48 (93.8%)	38/42 (90.5%)
MRSE, Attempted vs. Achieved, ±1.00D	4/4 (100.0%)	35/35 (100.0%)	52/52 (100.0%)	49/50 (98.0%)	48/48 (100.0%)	41/42 (97.6%)
MRSE, Attempted vs. Achieved, ±2.00D	4/4 (100.0%)	35/35 (100.0%)	52/52 (100.0%)	50/50 (100.0%)	48/48 (100.0%)	42/42 (100.0%)

Key Effectiveness Variables	Preop MRSPH				Total
	-6.01 to -7.00 D n/N (%)	-7.01 to -8.00 D n/N (%)	-8.01 to -9.00 D[1] n/N (%)	> -9.01 D[1] n/N (%)	n/N (%)
UCVA, 20/16 or better	25/42 (59.5%)	16/28 (57.1%)	4/15 (26.7%)	3/12 (25.0%)	197/328 (60.1%)
UCVA, 20/20 or better	36/42 (85.7%)	24/28 (85.7%)	9/15 (60.0%)	8/12 (66.7%)	287/328 (87.5%)
UCVA, 20/25 or better	39/42 (92.9%)	27/28 (96.4%)	13/15 (86.7%)	11/12 (91.7%)	313/328 (95.4%)
UCVA, 20/32 or better	42/42 (100.0%)	28/28 (100.0%)	15/15 (100.0%)	11/12 (91.7%)	322/328 (98.2%)
UCVA, 20/40 or better	42/42 (100.0%)	28/28 (100.0%)	15/15 (100.0%)	12/12 (100.0%)	327/328 (99.7%)
MRSE, Attempted vs. Achieved, ±0.25D	31/42 (73.8%)	16/28 (57.1%)	11/15 (73.3%)	6/12 (50.0%)	261/328 (79.6%)
MRSE, Attempted vs. Achieved, ±0.50D	38/42 (90.5%)	24/28 (85.7%)	14/15 (93.3%)	10/12 (83.3%)	305/328 (93.0%)
MRSE, Attempted vs. Achieved, ±1.00D	41/42 (97.6%)	27/28 (96.4%)	15/15 (100.0%)	11/12 (91.7%)	323/328 (98.5%)
MRSE, Attempted vs. Achieved, ±2.00D	42/42 (100.0%)	28/28 (100.0%)	15/15 (100.0%)	12/12 (100.0%)	328/328 (100.0%)

N = Number of CRFs received with non-missing values for each group. % = (n/N) x 100

[1] Please note that treatment of -8.01 to -10.0 D will present a flagged warning to the users so that the user understands that correction of these powers had not been substantiated by an adequate set of data.

The tables below summarize additional information related to the effectiveness results from the pivotal clinical trial.

Table 25. Postoperative Uncorrected Visual Acuity (UCVA) Compared to Preoperative Best Spectacle Corrected Visual Acuity (BSCVA) Effectiveness Cohort Eyes:

UCVA	Day 1 n	Day 1 (%)	Week 1 n	Week 1 (%)	Month 1 n	Month 1 (%)	Month 3 n	Month 3 (%)
Available (N)	333		332		333		331	
UCVA >2 Lines Better than Preop BSCVA	0	(0.0 %)	0	(0.0 %)	0	(0.0 %)	0	(0.0 %)
UCVA 2 Lines Better than Preop BSCVA	1	(0.3 %)	1	(0.3 %)	5	(1.5 %)	12	(3.6 %)
UCVA 1 Line Better than Preop BSCVA	10	(3.0 %)	20	(6.0 %)	56	(16.8 %)	71	(21.5 %)
UCVA Equal to Preop BSCVA	51	(15.3 %)	106	(31.9 %)	125	(37.5 %)	137	(41.4 %)
UCVA 1 Line Worse than Preop BSCVA	111	(33.3 %)	109	(32.8 %)	94	(28.2 %)	73	(22.1 %)
UCVA 2 Lines Worse than Preop BSCVA	86	(25.8 %)	56	(16.9 %)	31	(9.3 %)	25	(7.6 %)
UCVA >2 Lines Worse than Preop BSCVA	74	(22.2 %)	40	(12.0 %)	22	(6.6 %)	13	(3.9 %)
UCVA Better than or Equal to Preop BSCVA	62	(18.6 %)	127	(38.3 %)	186	(55.9 %)	220	(66.5 %)
Not reported	0		0		0		0	
Total	333		332		333		331	

UCVA	Month 6 n	Month 6 (%)	Month 9 n	Month 9 (%)	Month 12 n	Month 12 (%)
Available (N)	328		319		310	
UCVA >2 Lines Better than Preop BSCVA	1	(0.3 %)	1	(0.3 %)	3	(1.0 %)
UCVA 2 Lines Better than Preop BSCVA	12	(3.7 %)	4	(1.3 %)	13	(4.2 %)
UCVA 1 Line Better than Preop BSCVA	83	(25.3 %)	93	(29.2 %)	93	(30.0 %)
UCVA Equal to Preop BSCVA	133	(40.5 %)	132	(41.4 %)	119	(38.4 %)
UCVA 1 Line Worse than Preop BSCVA	67	(20.4 %)	59	(18.5 %)	57	(18.4 %)
UCVA 2 Lines Worse than Preop BSCVA	19	(5.8 %)	20	(6.3 %)	18	(5.8 %)
UCVA >2 Lines Worse than Preop BSCVA	13	(4.0 %)	10	(3.1 %)	7	(2.3 %)
UCVA Better than or Equal to Preop BSCVA	229	(69.8 %)	230	(72.1 %)	228	(73.5 %)
Not reported	0		0		0	
Total	328		319		310	

N = Number of CRFs received with non-missing values at each visit. % = (n/N) x 100

Accuracy of the intended refractive correction (IRC), with respect to manifest refractive spherical equivalent (MRSE), is shown in **Table 26** for the 6-month consistent effectiveness cohort. This cohort consists of all eyes from the effectiveness cohort with every follow-up exam from 1 week onward to the 6-month point of stability. The deviation of MRSE is considered in terms of a refractive target that is not necessarily emmetropia, due to the astigmatic components of 0.25 D and 0.50 D that were not treated in the study.

Table 26. Accuracy of MRSE — Attempted vs. Achieved 6-Month Consistent Effectiveness Cohort:

MRSE Deviation	Week 1 n/N (%)	Month 1 n/N (%)	Month 3 n/N (%)
Available (N)	326	327	327
± 0.25 D	257/326 (78.8%)	259/327 (79.2%)	258/327 (78.9%)
± 0.50 D	303/326 (92.9%)	304/327 (93.0%)	300/327 (91.7%)
± 1.00 D	323/326 (99.1%)	325/327 (99.4%)	324/327 (99.1%)
± 2.00 D	326/326 (100.0%)	327/327 (100.0%)	327/327 (100.0%)
Overcorrected > 1.00 D	0/326 (0.0%)	0/327 (0.0%)	0/327 (0.0%)
Overcorrected > 2.00 D	0/326 (0.0%)	0/327 (0.0%)	0/327 (0.0%)
Undercorrected > 1.00 D	3/326 (0.9%)	2/327 (0.6%)	3/327 (0.9%)
Undercorrected > 2.00 D	0/326 (0.0%)	0/327 (0.0%)	0/327 (0.0%)
Mean (SD)	0.035 (0.311)	0.054 (0.301)	0.062 (0.328)
Range	-1.000, 1.375	-1.000, 1.375	-0.875, 1.875
Not reported	1	0	0
Total	327	327	327

MRSE Deviation	Month 6 n/N (%)	Month 9 n/N (%)	Month 12 n/N (%)
Available (N)	327	316	307
± 0.25 D	260/327 (79.5%)	256/316 (81.0%)	248/307 (80.8%)
± 0.50 D	304/327 (93.0%)	300/316 (94.9%)	288/307 (93.8%)
± 1.00 D	322/327 (98.5%)	313/316 (99.1%)	303/307 (98.7%)
± 2.00 D	327/327 (100.0%)	316/316 (100.0%)	307/307 (100.0%)
Overcorrected > 1.00 D	0/327 (0.0%)	0/316 (0.0%)	0/307 (0.0%)
Overcorrected > 2.00 D	0/327 (0.0%)	0/316 (0.0%)	0/307 (0.0%)
Undercorrected > 1.00 D	5/327 (1.5%)	3/316 (0.9%)	4/307 (1.3%)
Undercorrected > 2.00 D	0/327 (0.0%)	0/316 (0.0%)	0/307 (0.0%)
Mean (SD)	0.041 (0.325)	0.023 (0.292)	0.017 (0.309)
Range	-0.750, 1.750	-0.875, 1.250	-1.000, 1.750
Not reported	0	0	0
Total	327	316	307

N = Number of CRFs received with non-missing values at each visit. % = (n/N) x 100

3. Subgroup Analyses

   Stratification by age revealed differences in proportions of eyes achieving UCVA of 20/20 or better, with lower proportions of eyes in the 40 to 49 and 50+ age groups achieving UCVA of 20/20 or better at the point of stability (72.0% for the 40 to 49 years subgroup and 71.4% for the 50 years & above subgroup). Despite these slight differences, the older age groups still experienced a clinically significant visual benefit as 98.4% of the subjects in these age bins achieved UCVA of 20/40 or better postoperatively.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 6 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c),

and (f). The information provided does not raise any questions about the reliability of the data.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Ophthalmic Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

There were no eyes with preoperative UCVA of 20/40 or better. At the refractive time point of stability of 6 months postoperatively, 99.7% (327/328) and 87.5% (287/328) achieved uncorrected visual acuity of 20/40 or better and 20/20 or better, respectively, with no subjects having best corrected visual acuity worse than 20/40 at their last available visit. Similar results were achieved at the 12-month visit.
Additionally, the MRSE was within ±1.00 D of attempted correction in over 98 % of eyes at all study visits. No fewer than 79 % of eyes were within ±0.25 D, and no fewer than 92 % of eyes were within ±0.50 D of the targeted MRSE correction from the 1-week through 12-month visits. There were no reports of overcorrection > 1.00 D MRSE at any point in the study.

The pivotal clinical trial outcomes support the reasonable assurance of the effectiveness of the device for the proposed indications for use.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies as well as data collected in the pivotal clinical study conducted to support PMA approval, as described above. No study subject presented with a loss of ≥ 2 lines BSCVA, with BSCVA worse than 20/40, or with increased manifest refractive astigmatism > 2.00 D at 6 months or at the last available visits. With regard to loss of ≥ 2 lines BSCVA at any point during the study, there were 19 study eyes at Week 1, 5 eyes at Month 1, and 3 eyes at interim visits with this degree of loss. A total of 14 subjects were reported with 15 ocular adverse events (AEs) over the course of the study. No AE occurred at a rate of 1% or greater per type of event. There were an additional 15 intraoperative complications. Postoperative complications included moderate to severe visual symptoms of glare (10.4%) and haloes (6.0%), interface debris (2.7%), dry eye syndrome (2.7%), diffuse lamellar keratitis (0.9%), epithelium in the interface (0.9%), corneal striae (0.3%), and 1 report each (0.3%) of foreign body sensation at 1 month or later, pain at 1 month or later, and transient light sensitivity

syndrome. In the majority of cases, harmful events resolved without severe residual sequelae.

The pivotal clinical study outcomes support the reasonable assurance of the safety of the device for the proposed indications for use.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in the clinical study conducted to support PMA approval as described above.

While there were no eyes preoperatively with UCVA of 20/40 or better, at the refractive time point of stability of 6 months postoperatively, 99.7% (327/328) and 87.5% (287/328) achieved uncorrected visual acuity of 20/40 or better and 20/20 or better, respectively, with no subjects having best corrected visual acuity worse than 20/40 at their last available visit. Similar results were achieved at the 12-month visit.

The potential risks are mitigated by the labeling.

Patient perspectives considered during the review included a questionnaire that was administered during the clinical trial to collect information on patient symptoms. However, the modified QoV used in this trial could not be determined to be a reliable measure of visual symptoms by the FDA. Therefore, caution must be used in interpreting the data, given that the reported prevalence and severity of symptoms may not be accurate.

In conclusion, given the available information above, the data support that, for small incision lenticule extraction (SMILE) for the reduction or elimination of myopia $\geq$ -1.00 D to $\leq$ -8.00 D, with $\leq$ -0.50 D cylinder and MRSE $\leq$ -8.25 D in the eye to be treated in patients who are 22 years of age or older with documentation of stable manifest refraction over the past year as demonstrated by a change of $\leq$ 0.50 D MRSE, the probable benefits of the device outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

The benefit of the device for the indications for use, as demonstrated by the uncorrected distance visual acuity results of the pivotal clinical trial, outweigh the potential risks.

XIII. CDRH DECISION

CDRH issued an approval order on September 13, 2016.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.