SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Ophthalmic Excimer Laser System
Device Trade Name:	STAR S4 IR™ Excimer Laser System iDesign Advanced WaveScan Studio™ System
Device Procode:	LZS
Applicant's Name and Address:	AMO Manufacturing USA, LLC. 510 Cottonwood Drive Milpitas, CA 95035
Date(s) of Panel Recommendation:	None

Premarket Approval (PMA) Application Number: P930016/S044

Date of FDA Notice of Approval: May 6, 2015

The sponsor submitted this supplement to further expand the Star S4 IR Excimer Laser System indications for use to include reduction or elimination of myopic astigmatism up to -11.00 D spherical equivalent, and up to 5.00 D cylinder, as measured by the iDesign Advanced WaveScan Studio system. The updated clinical data to support the expanded indication is provided in this summary. The preclinical test results were presented in the original PMA application. The SSEDs to support the approved indications are available on the CDRH website.

II. INDICATIONS FOR USE

The STAR S4 IR Excimer Laser System and iDesign Advanced WaveScan Studio System is indicated for wavefront-guided laser assisted in situ keratomileusis (LASIK) in patients:

- with myopia as measured by the iDesign Advanced WaveScan Studio system up to -11 D spherical equivalent with up to -5 D cylinder
- with agreement between manifest refraction (adjusted for optical infinity) and iDesign Advanced WaveScan Studio System refraction as follows:
  - Spherical Equivalent: Magnitude of the difference is less than 0.625 D.
  - Cylinder: Magnitude of the difference is less than or equal to 0.5 D.
- 18 years of age or older, and

▪ with refractive stability (a change of ≤1.0 D in sphere or cylinder for a minimum of 12 months prior to surgery).

III. CONTRAINDICATIONS

Laser refractive surgery is contraindicated:

- in patients with collagen vascular, autoimmune or immunodeficiency diseases.
- in pregnant or nursing women
- in patients with signs corneal abnormalities including signs of keratoconus, abnormal corneal topography, epithelial basement membrane disease (EBMD) or degenerations of the structure of the cornea.
- in patients with symptoms of significant dry eye. If the patients have severely dry eyes, LASIK may increase the dryness. This may or may not go away. Severe eye dryness may delay healing of the flap or interfere with the surface of the eye after surgery. It may result in poor vision after LASIK.
- in patients whose corneal thickness would cause the anticipated treatment would violate the posterior 250 microns (μ m) of corneal stroma.
- in patients with advanced glaucoma.
- in patients with uncontrolled diabetes.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the STAR S4 IR Excimer Laser System and iDesign Advanced WaveScan Studio System labeling.

V. DEVICE DESCRIPTION

1. iDesign Advanced WaveScan Studio System

The iDesign Advanced WaveScan Studio System incorporates wavefront aberrometry, auto-refraction, corneal topography, keratometry, and pupillometry. The System measures the refractive error and wavefront aberrations of the human eye using a high-definition Hartmann-Shack wavefront sensor. The measurements can be used to determine regular (sphero-cylindrical) refractive errors and irregularities (aberrations) that cause decreased or blurry vision in the human eye.

The function of the Hartmann-Shack sensor is to measure the refractive error of the eye by evaluating the deflection of rays emanating from a small beam of light projected onto the retina. To control the natural accommodation of the eye during iDesign Advanced WaveScan Studio system imaging, the system incorporates a fogged fixation target.

The iDesign Advanced WaveScan Studio System optical head projects a beam of light onto the retina. The light reflects back through the optical path of the eye and into the wavefront device. The reflected beam is imaged by a lenslet array onto the charge-coupled device (CCD). Each lens of the array gathers light information (deflection information) from a different region of the pupil to form an image of the light that passes through that region of the pupil. An array of spots is imaged on the CCD sensor. The system compares the locations of the array of spots gathered from the CCD to the theoretical ideal (the ideal plane wave).

The iDesign Advanced WaveScan Studio System software uses these data to compute the eye's refractive errors and wavefront aberrations using Fourier Transform analysis. The system displays the refractive errors and wavefront aberrations as the optical path difference (OPD) between the measured outgoing wavefront and the ideal plane wave. The iDesign Advanced WaveScan Studio system software subtracts the refractive errors from the wavefront errors map and displays the higher order aberrations as OPD errors. Regions of the pupil with positive OPD are in front of the ideal plane wave and areas with negative OPD are behind the ideal plane wave.

2. STAR S4 IR Excimer Laser System

The STAR S4 IR laser system is a 193 nm excimer laser system that delivers spatially scanning ultraviolet pulses of variable shapes and sizes on to the cornea. Pulse shapes may be circles of variable diameter or slits of variable width and orientation. The range of diameters and slit widths available during treatments is 0.65 mm to 6.5 mm. An auto-centering dual camera infrared eye tracking system (ActiveTrak), together with the delivery system, aligns the treatment to the eye, and compensates for eye movements during laser correction to maximize the corneal reshaping accuracy. An operating microscope is used to observe the patient procedures and to facilitate accurate focus and laser beam alignment. A debris-removal system is designed to evacuate the debris plume that occurs during ablation. The operating chair and fixation LED align the patient, while a video camera and monitor records the patient treatment. The variable spot scanning (VSS) feature of the laser, used for Advanced CustomVue treatments delivers variable diameter ultraviolet pulses to precise locations by the scanning delivery system. The VSS algorithm optimizes the ablation pattern by choosing the best combination of beam diameters and locations to achieve a target shape.

Features and components of the STAR S4 IR System include:

- Excimer Laser
- Gas Management System
- Laser Beam Delivery System
- Patient Management System
- Computer Control
- AMO Treatment Card

3. Microkeratome

The Advanced CustomVue procedure required the use of a commercially available keratome that has been cleared for marketing via premarket notification. The keratomes used in this study consisted of femtosecond ophthalmic surgical lasers that create a LASIK flap through precise individual microphotodisruptions of tissue, created by tightly focused ultrashort pulses which are delivered through a disposable applanation lens while fixating the eye under very low vacuum.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative methods of correcting of visual correction include: glasses, contact lenses, phakic intraocular lenses, conventional LASIK, topography guided LASIK and photorefractive keratectomy (PRK).

Each alternative has its own advantages and disadvantages. A prospective patient should fully discuss with his/her care provider these alternatives in order to select the correction method that best meets his/her expectation and lifestyle.

VII. MARKETING HISTORY

The iDesign Advanced WaveScan Studio system has been marketed in approximately 40 countries including; Algeria, Australia, Austria, Belgium, Brazil, Bulgaria, Canada, Chile, Colombia, Czech Republic, Denmark, Egypt, Finland, France, Germany, Great Britain, India, Indonesia, Iraq, Ireland, Italy, Japan, Jordan, Malaysia, Mexico, the Netherlands, New Zealand, Poland, Qatar, Singapore, Saudi Arabia, South Africa, South Korea, Spain, Taiwan, Tunisia, Turkey, United Arab Emirates and Yemen. The STAR S4 IR Excimer Laser system is on market in 70 countries. Neither device has been withdrawn from any country or market for reasons of safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse reactions associated with LASIK include: loss of best spectacle corrected visual acuity (BSCVA), worsening of patient complaints such as double vision, sensitivity to bright lights, increased difficulty with night vision, fluctuations in vision, increase in intraocular pressure, corneal haze, secondary surgical intervention, corneal infiltrate or ulcer, corneal epithelial defect, corneal edema, problems associated with the flap including a lost, misplaced or misaligned flap, retinal detachment, and retinal vascular accidents.

Please refer to the complete listing of adverse events and complications observed during the clinical study which are presented in Tables 8 and 9 of the Summary of Clinical Studies section below.

IX. SUMMARY OF PRECLINICAL STUDIES

For a summary of non-clinical studies (excluding hazard analysis and software testing) for the STAR S4 IR Excimer Laser System, please refer to the SSED of the original PMA P930016.

Preclinical studies performed demonstrate the safety and effectiveness of the iDesign Advanced WaveScan Studio system. The results of these studies are summarized below.

1. Hazard Analysis and Software Validation

   Fault tree and failure mode and effects analyses were conducted to evaluate pre- and post-mitigation hazards along with the potential severity of harm resulting from these hazards. All risks and harms analyzed are determined to be acceptable when evaluated against the potential benefits of the system. Mitigation of hazards have reduced the final risk acceptability ratings to as low as possible (ALAP). Preclinical software and system verification and validation testing was performed according to pre-approved protocols to demonstrate functionality and performance to all requirements and risk mitigations. All tests were successfully completed; all items tested during verification and validation testing met the acceptance criteria.

2. Refraction Accuracy and Repeatability
   Accuracy and repeatability of the wavefront-derived sphere and cylinder were tested and met the requirement of ±0.1 D and repeatability of 0.04 D (one standard deviation). This verification was performed by measuring a set of known trial lenses. Additionally, the refraction accuracy (sphere, cylinder and axis) was verified with the optical axis of the instrument up to ± 1mm off from the center of the pupil. The accuracy of the measurement of high order aberrations (3^{rd} through 6^{th} Zernike order) were confirmed to be accurate to within ± 0.08µm.

3. Keratometry Accuracy
   Accuracy of keratometry measurements was demonstrated by measuring the sphericity of known steel spheres and toroidal test eyes characterized using an on-market topographer.

4. Pupillometry Accuracy
   Accuracy of pupil diameter measurements was tested and verified to be accurate to ≤ 0.15 mm using model eyes with known pupil diameters.

X. SUMMARY OF PRIMARY CLINICAL STUDY

A. Study Design

The safety and effectiveness of wavefront-guided LASIK correction of myopic refractive errors with the iDesign Advanced WaveScan Studio System and STAR S4 IR Excimer Laser System has been evaluated in a clinical investigation. The study was a 2-year, prospective, multicenter, open-label, non-randomized clinical investigation of up to 345 eyes (of up to 345 subjects).

Subjects who agreed to participate provided informed consent and underwent the required screening procedures to determine eligibility. To qualify for enrollment, subjects were to meet all eligibility criteria for one or both eyes. In general, eyes were to be healthy with iDesign Advanced WaveScan Studio system measured myopic refractive error (with or without astigmatism) of sphere of up to -12.00 D, cylinder between 0.00 and -8.00 D, and with a maximum spherical equivalent of -12.00 D.

i. Subject Inclusion Criteria

- At least 18 years of age and give written informed consent.
- Myopic refractive error with or without astigmatism with sphere up to -12.00 D, and cylinder between 0.00 and -8.00 D with a maximum spherical equivalent (SE) of -12.00 D.
- Anticipated postoperative stromal bed thickness of at least 250 microns.
- BSCVA of 20/20 or better.
- UCVA of 20/40 or worse.
- Less than or equal to 0.75 D difference between cycloplegic and manifest refraction sphere.
- A stable refractive error over the last 12 months as defined by a change of ≤1.00 D in sphere or cylinder.
- Demonstration of refractive stability for subjects who wear contact lenses: rigid or toric lenses must be removed for at least 3 weeks and soft contact lenses for at least 1 week prior to the first refraction to establish stability.
- Agreement between manifest refraction (adjusted for optical infinity) and iDesign Advanced WaveScan Studio System refraction chosen for treatment.

ii. Subject Exclusion Criteria

- Women who are pregnant, breast-feeding, or intend to become pregnant over the course of the study, as determined by verbal inquiry.

- Concurrent use of systemic (including inhaled) medications that may impair healing (e.g., corticosteroids).

- History of any of the following medical conditions, or any other condition that could affect wound healing: collagen vascular disease, autoimmune disease, immunodeficiency diseases, ocular herpes zoster or herpes simplex, endocrine disorders (including, but not limited to, unstable thyroid disorders and diabetes), lupus, rheumatoid arthritis, and diabetes (regardless of type, duration, severity or control).

- Subjects with a cardiac pacemaker, implanted defibrillator or other implanted electronic device.

- History of prior intraocular or corneal surgery (including cataract extraction), active ophthalmic disease or abnormality (including, but not limited to, symptomatic blepharitis, recurrent corneal erosion, dry eye syndrome, neovascularization > 1 mm from limbus), retinal detachment/repair, clinically significant lens opacity, clinical evidence of trauma, corneal opacity within the central 9 mm and visible on topography, at risk for developing strabismus, or with evidence of glaucoma or propensity for narrow angle glaucoma.

- Evidence of keratoconus, corneal dystrophy or irregularity, or abnormal topography.

1. Follow-up Schedule and Study Procedures

All eyes were evaluated according to the schedule below.

Clinical Study Visit Schedule

EXAM		VISIT WINDOW
Preoperative Evaluation		
Operative		1-120 days following preoperative exam
1 Day	Postoperative Exam	12-26 hours postoperative
1 Week	Postoperative Exam	5-9 days postoperative
1 Month	Periodic Exam	3-5 weeks postoperative
3 Months	Periodic Exam	10-14 weeks postoperative
6 Months	Periodic Exam	21-26 weeks postoperative
9 Months	Periodic Exam	35-43 weeks postoperative
12 Months	Periodic Exam	11-14 months postoperative
24 Months	Periodic Exam	23-27 months postoperative

Study procedures included uncorrected distance visual acuity, best spectacle corrected distance visual acuity, contrast sensitivity, manifest refraction, cycloplegic refraction, keratometry, intraocular pressure, corneal pachymetry, corneal topography, iDesign Advanced WaveScan Studio System measurements, slit-lamp evaluation of the anterior segment, subjective questionnaires, and determination of adverse events and complications. Treatment plans were based on preoperative iDesign Advanced WaveScan Studio system measurements and all eyes were targeted for emmetropia.

2. Clinical Endpoints

The key safety and effectiveness endpoint targets, evaluated at the time of refractive stability, are:

i. Safety Endpoint Targets

a) PRIMARY: <5% of eyes with a loss of >2 lines of best spectacle corrected visual Acuity (BSCVA)

b) <1% of eyes with a BSCVA of 20/20 or better preoperatively that have a BSCVA of worse than 20/40 (Note: All eyes had to have BSCVA of 20/20 or better for study inclusion.)

c) <5% of eyes with induced manifest refractive astigmatism >2.00 diopters (D)

d) <1% of eyes with an adverse event (serious, non-flap related)

ii. Effectiveness Endpoint Targets

a) PRIMARY: 85% of eyes with an uncorrected visual acuity (UCVA) of 20/40 or better

b) 50% of eyes with a manifest refractive spherical equivalent (MRSE) within 0.50 D of intended correction.

c) 75% of eyes with an MRSE within 1.00 D of intended correction

d) 95% of eyes achieve refractive stability

Other endpoints included contrast sensitivity, higher order aberrations, complications, directed visual symptoms assessment, National Eye Institute-Refractive Error Quality of Life (NEI-RQL-42) visual functioning and visual wellbeing questionnaire results, keratometric analyses, and vector and non-vector analyses of manifest refractive cylinder. The key outcome variables were assessed postoperatively at the periodic exams. Refractive stability was achieved at 6 months; therefore, the key safety and effectiveness study endpoints were evaluated at 6 months as the primary study analysis.

No retreatments were performed in the study. Therefore, no safety or effectiveness data are available for the use of the iDesign Advanced WaveScan Studio System and STAR S4 IR Excimer Laser System in performing a retreatment procedure or for eyes with primary LASIK treatment in this study that have a retreatment performed using another technology.

iii. Statistical Methods

Descriptive statistics (including sample size (n), mean, standard deviation (SD), minimum, maximum, as appropriate) and frequency distributions were used to summarize clinical outcomes. Confidence intervals for binomial proportions were computed using the Clopper-Pearson Exact method. All confidence intervals, statistical tests and resulting p-values were reported as two-sided and assessed at a 0.05 significance level.

For analysis of refractive outcomes, the sphere component of the manifest refraction (as tested at 4.0 m) was adjusted for optical infinity by adding -0.25 D to the sphere magnitude. Similarly, manifest refraction spherical equivalent (MRSE) was calculated using the adjusted manifest sphere value. Additionally, all refractions were converted to minus cylinder format and adjusted for vertex distance (standardized to 12.5 mm).

B. Accountability of PMA Cohort

A total of 170 subjects had one or both eyes treated for a total of 334 treated eyes across 12 clinical sites in the U.S. The majority of subjects were bilaterally treated; 164 subjects

(96.5%; 164/170) had both eyes treated and six subjects (3.5%; 6/170) had a single eye treated.

Table 1 presents the accountability to date for the 334 eyes treated in this study. Subject compliance was excellent with a percent accountability of 100% (334/334) through 6 months. Although the study is ongoing, a substantial portion of eyes completed both the 9-month (95.8%, 320/334) and 12-month study visits (87.4%, 292/334).

TABLE 1

Accountability of All Treated Eyes (N=334)

	Postop Exams (Safety)				**Periodic Study Exams**									
	1 Day		**1 Week**		**1 Month**		**3 Months**		**6 Months**		**9 Months**		**12 Months**	
Status	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Available for Analysis	**334**	**100**	**334**	**100**	**334**	**100**	**334**	**100**	**334**	**100**	**320**	**95.8**	**292**	**87.4**
--Out of Interval	0	0.0	4	1.2	8	2.4	6	1.8	12	3.6	2	0.6	2	0.6
Missing Subjects	**0**	**0.0**	**0**	**0.0**	**0**	**0.0**	**0**	**0.0**	**0**	**0.0**	**14**	**4.2**	**42**	**12.6**
--In interval or past interval[a]	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
--Active (not yet in visit interval)	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	12	3.6	42	12.6
--Missed visit	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	2	0.6	0	0.0
--Lost-to-Follow-Up	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0[b]	0.0
--Discontinued	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

[a] Form not yet received

[b] Four eyes (2 subjects) were lost-to-follow-up after completion of the 12-month visit.

% = n/N(100)

C. Study Population Demographics and Baseline Parameters

Subject demographics are presented in **Table 2**. The mean age of the study population was 32.3 years (SD 8.3; range 18 to 58) and the majority of subjects were Caucasian (66.5%). Subjects at the 5 clinical sites located in California and the Southwest were primarily Caucasian and Hispanic, whereas subjects at the clinical sites elsewhere in the USA were primarily Caucasian.

TABLE 2

Demographic Characteristics
N=170

Category	Classification	n (%)
Gender	Male	93 (54.7%)
	Female	77 (45.3%)
Race	Caucasian	113 (66.5%)
	Black/African Descent	5 (2.9%)
	Native American/Inuit	0 (0.0%)
	Asian	10 (5.9%)
	Pacific Islander	3 (1.8%)
	Other[a]	39 (22.9%)
Age (Years)	Mean	32.3
	SD	8.31
	Min	18
	Max	58
Contact Lens History	None	49 (28.8%)
	Soft	71 (41.8%)
	Rigid/Toric	50 (29.4%)

[a] Hispanic, Caucasian/Asian, Caucasian/Hispanic, Eurasian, Hispanic/Italian, Indian
%=n/N(100)

Table 3 presents the mean preoperative manifest and ***iDesign Advanced WaveScan Studio*** system measured refractive error for the 334 treated eyes. Mean preoperative refractive measurements were comparable between manifest refraction and ***iDesign Advanced WaveScan Studio*** system refraction.

TABLE 3

Mean Preoperative Manifest and *iDesign AWS* Refractive Error in Diopters

All Eyes (N=334)

Refractive Variable	Mean	Std Dev	Median	Min	Max
Manifest Refraction Spherical Equivalent (MRSE)	-6.21	2.78	-5.99	-12.13	-1.25
***iDesign AWS* Spherical Equivalent (IDSE)**	-6.15	2.81	-5.91	-11.98	-1.04

Tables 4 and **5** present the preoperative refractive error bin distributions for the study population based on preoperative ***iDesign Advanced WaveScan Studio*** system measurements. Indicated treatment ranges are represented by un-shaded areas of **Tables 4** and **5** (with more than 20 eyes per category); however eyes in all refractive bins were studied.

TABLE 4

Preoperative Refractive Error by *iDesign AWS* Sphere and Cylinder

All Eyes (N=334)

	***iDesign AWS* Cylinder**									
***iDesign AWS* Sphere**	**0 to ≤-0.5 D**	**>-0.5 to ≤-1 D**	**>-1 to ≤-2 D**	**>-2 to ≤-3 D**	**>-3 to ≤-4 D**	**>-4 to ≤-5 D**	**>-5 to ≤-6 D**	**>-6 to ≤-7 D**	**>-7 to ≤-8 D**	**Total**
≥ 0 to ≤ -1 D	0	1	5	4	6	2	2	2	0	**22**
>-1 to ≤-2 D	10	4	0	2	6	5	3	2	0	**32**
>-2 to ≤-3 D	8	2	8	4	1	3	3	1	0	**30**
>-3 to ≤-4 D	14	6	5	3	5	8	0	0	0	**41**
>-4 to ≤-5 D	14	5	11	7	6	4	1	0	1	**49**
>-5 to ≤-6 D	3	8	6	5	2	2	1	0	1	**28**
>-6 to ≤-7 D	8	12	6	5	1	0	0	0	0	**32**
>-7 to ≤-8 D	4	7	8	8	1	0	0	0	0	**28**
>-8 to ≤-9 D	6	8	2	3	3	0	0	0	0	**22**
>-9 to ≤-10 D	9	3	4	4	1	2	0	0	0	**23**
>-10 to ≤-11 D	6	6	5	2	2	0	0	0	0	**21**
>-11 to ≤-12 D	5	1	0	0	0	0	0	0	0	**6**
Total	**87**	**63**	**60**	**47**	**34**	**26**	**10**	**5**	**2**	**334**

Treatment of diopter ranges indicated by shaded rows and columns is locked out by *AMO* Treatment Card

TABLE 5

Preoperative Refractive Error by *iDesign AWS* Spherical Equivalent (SE) and Cylinder

All Eyes (N=334)

	***iDesign AWS* Cylinder**									
iDesign AWS SE	**0 to ≤-0.5 D**	**>-0.5 to ≤-1 D**	**>-1 to ≤-2 D**	**>-2 to ≤-3 D**	**>-3 to ≤-4 D**	**>-4 to ≤-5 D**	**>-5 to ≤-6 D**	**>-6 to ≤-7 D**	**>-7 to ≤-8 D**	**Total**
>-1 to ≤-2 D	9	2	5	4	2	0	0	0	0	**22**
>-2 to ≤-3 D	9	5	4	1	6	2	0	0	0	**27**
>-3 to ≤-4 D	12	5	6	5	4	5	2	1	0	**40**
>-4 to ≤-5 D	15	5	6	3	3	3	5	2	0	**42**
>-5 to ≤-6 D	4	6	11	6	5	8	1	2	0	**43**
>-6 to ≤-7 D	6	9	6	5	6	4	0	0	0	**36**
>-7 to ≤-8 D	6	10	4	6	1	2	2	0	0	**31**
>-8 to ≤-9 D	5	10	7	7	0	0	0	0	2	**31**
>-9 to ≤-10 D	9	4	4	3	3	0	0	0	0	**23**
>-10 to ≤-11 D	7	5	6	5	1	0	0	0	0	**24**
>-11 to ≤-12 D	5	2	1	2	3	2	0	0	0	**15**
Total	**87**	**63**	**60**	**47**	**34**	**26**	**10**	**5**	**2**	**334**

Treatment of diopter ranges indicated by shaded rows and columns is locked out by *AMO* Treatment Card

D. Safety and Effectiveness Results

i. Safety Results

The analysis of safety was based on the cohort of all myopic eyes available at 6 months postoperative (334/334 eyes). A summary of key safety variables over time is presented in **Table 6** for all myopic eyes.

a) Less than 5% of eyes with a loss of >2 lines BSCVA: At 6 months, no eyes (0.0%; 0/334) had a decrease in BSCVA of >2 lines meeting the primary study endpoint safety target of <5% of eyes with a loss of >2 lines of BSCVA. One eye (0.3%; 1/334) had a transient decrease in BSCVA of 2 lines at 6 months (20/10 preoperative to 20/16 at 6 months; improved to 20/12.5 at 9 months).

b) *Less than 1% of eyes with a BSCVA of 20/20 or better preoperatively that have a BSCVA of worse than 20/40:* No eyes (0%; 0/334) had preoperative BSCVA of 20/20 or better but worse than 20/40 postoperatively at any time during the study, meeting the safety endpoint target of <1% of eyes with preoperative BSCVA of 20/20 or better having BSCVA worse than 20/40 postoperatively.

c) *Less than 5% of eyes with induced manifest refractive astigmatism >2.00 diopters:* At 6 months, only one eye (#7082; 0.3%, 1/334) had an increase in absolute manifest refractive cylinder of >2.00 D (-2.25 D), meeting the safety criterion of <5% of eyes with induced manifest refractive cylinder >2.00 D.

TABLE 6

Key Safety Variables Over Time

Safety Variable	1 Week (N=334) n	%	1 Month (N=334) n	%	3 Months (N=334) n	%	6 Months (N=334) n	%	9 Months (N=320) n	%	12 Months (N=290) n	%
Loss of >2 lines BSCVA[a]	1	0.3%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Loss of ≥2 lines BSCVA	8	2.4%	1	0.3%	0	0.0%	1	0.3%	0	0.0%	0	0.0%
BSCVA 20/16 or better	249	74.6%	286	85.6%	298	89.2%	303	90.7%	289	90.3%	267	92.1%
BSCVA 20/20 or better	323	96.7%	331	99.1%	333	99.7%	334	100%	319	99.7%	290	100%
BSCVA 20/25 or better	332	99.4%	334	100%	334	100%	334	100%	320	100%	290	100%
BSCVA worse than 20/40[b]	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Induced Manifest Cylinder >2.0 D[c]	0	0.0%	0	0.0%	1	0.3%	1	0.3%	0	0.0%	0	0.0%

[a] **Safety endpoint target**: <5% of eyes with loss of >2 lines BSCVA vs. preoperative

[b] **Safety endpoint target:** <1% of eyes with BSCVA of 20/20 or better preoperative have BSCVA of worse than 20/40 postoperative. All eyes had preoperative BSCVA of 20/20 or better.

[c] **Safety endpoint target:** <5% of eyes with induced manifest refractive astigmatism >2.00 D

% = n/N(100)

d) *BSCVA Preservation*

The change in lines of BSCVA postoperatively compared to preoperatively for all myopic eyes is presented in **Table 7**. At 6 months, 55.7% (186/334) of eyes had at least a line improvement in BSCVA compared to preoperative. No eyes were reported with a loss of ≥2 lines of BSCVA at unscheduled visits.

TABLE 7

Change in BSCVA Over Time vs. Preoperative All Myopic Eyes

Acuity Change	1 Week n	%	1 Month n	%	3 Months n	%	6 Months n	%	9 Months n	%	12 Months n	%
>2 line increase	0	0.0%	1	0.3%	1	0.3%	0	0.0%	2	0.6%	0	0.0%
2 line increase	12	3.6%	16	4.8%	22	6.6%	25	7.5%	32	10.0%	18	6.2%
1 line increase	104	31.1%	143	42.8%	169	50.6%	161	48.2%	139	43.4%	143	49.3%
No change	172	51.5%	155	46.4%	129	38.6%	143	42.8%	136	42.5%	121	41.7%
1 line decrease	38	11.4%	18	5.4%	13	3.9%	4	1.2%	11	3.4%	8	2.8%
2 line decrease	7	2.1%	1	0.3%	0	0.0%	1[a]	0.3%	0	0.0%	0	0.0%
>2 line decrease	1	0.3%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
All N (%)	334	100.0%	334	100.0%	334	100.0%	334	100.0%	320	100.0%	290	100.0%

Acuity Change	1 Week		1 Month		3 Months		6 Months		9 Months		12 Months	
	n	%	n	%	n	%	n	%	n	%	n	%

[a] One eye had a transient decrease in BSCVA of 2 lines from preoperative BSCVA of 20/10 to 20/16 at 6 months; BSCVA improved to 20/12.5 at 9 months.

% = n/N(100)

e) *Adverse Events*

A summary of adverse events that occurred during the study are presented in **Table 8**. Five adverse events were considered serious (vision threatening): 2 cases of primary open angle glaucoma (of the same subject), 2 cases of TLSS (of the same subject), and 1 case of melting of the flap.

Less than 1% of eyes with an adverse event (serious, non-flap related): The 2 cases of primary open angle glaucoma and the 2 cases of TLSS were considered serious, non-flap related, adverse events for a rate of 1.2% (4/334). Although this rate of 1.2% is slightly above the 1% safety criterion for serious, ocular (non-flap) related events, it is not statistically significantly higher (p=0.7166) than the target value, and the individual rates of each event type (0.6%; 2/334) are below the 1% criterion. Additionally, as only the 2 cases of serious TLSS were considered device-related, the rate of serious, non-flap, device-related adverse events is less than 1% (0.6%; 2/334).

TABLE 8

Summary of Adverse Events Over Time

All Eyes (N=334)

Complication	<1 Month (N=334) n	%	1 Month (N=334) n	%	3 Months (N=334) n	%	6 Months (N=334) n	%	9 Months (N=320) n	%	12 Months (N=292) n	%	Cumulative (N=334) n	%
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
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
Corneal edema at 1 month or later (specify "flap", "bed", or both)			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
Miscreated flap (decentered, lost, incomplete, too thin, or other)	1[a]	0.3[a]	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1[a]	0.3[a]
Melting of the flap	0	0.0	0	0.0	0	0.0	1[b]	0.3	1[b]	0.3	1[b]	0.3	1[b]	0.3
IOP with increase >10 mmHg above baseline on two consecutive examinations or an IOP >30 mmHg on two consecutive examinations	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)							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
Severe glare, dry eye, or halos at 3 months or later					2[c]	0.6	0	0.0	0	0.0	0	0.0	2[c]	0.6
Decrease in BSCVA of greater than or equal to 2 lines (≥10 letters) not due to irregular astigmatism, at 3 months or later					0	0.0	1[d]	0.3	0	0.0	0	0.0	1[d]	0.3
Any other vision-threatening event	0	0.0	2[e]	0.6	0	0.0	2[f]	0.6	2[f]	0.6	2[f]	0.7	4[e,f]	1.2
Diffuse Lamellar Keratitis (DLK, grade 3 or above)	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Retinal detachment	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

Note: Shaded areas represent time frames outside event definition.

[a] One eye was unable to be treated due to incomplete flap (unable to be lifted) and not included in treated study cohort; incidence 0.3%; 1/335.

[b] One eye was reported with adverse event of melting of the flap beginning at 6 months; UCVA 20/16 at 12 months.

[c] Two eyes (of same subject) reported with adverse events of severe dryness at 3 months; resolution prior to 6 months. In addition, 4 subjects (2.4%; 4/170) in the study reported being very bothered by glare with marked severity.

[d] One eye reported with a transient 2-line loss in BSCVA vs. preoperative. BSCVA was 20/16 at 6 months vs. 20/10 preoperative; improved to 20/12.5 at 9 months.

[e] Two eyes (of same subject) reported with serious (sight-threatening) Transient Light Sensitivity Syndrome (TLSS); resolution prior to 3 months.

[f] Two eyes (of same subject) reported with serious (sight-threatening) primary open angle glaucoma.

% = n/N(100)

f) *Complications*

Complications that occurred during the study are presented in **Table 9**. Complications are defined as anticipated, transient, and non-sight-threatening events. There were no reports of corneal epithelial defects, corneal edema or diffuse lamellar keratitis at 1 month or later. There were reports of epithelium in the interface (epithelial ingrowth; 2.7% at 6 months) but all were either trace or mild in severity and none required removal. There were also reports of foreign body sensation and pain at 1 month or later (4%-5% at 6 months) but most of these were mild.

TABLE 9

Summary of Complications Over Time

All Eyes (N=334)

Complication	<1 Month (N=334)		1 Month (N=334)		3 Months (N=334)		6 Months (N=334)		9 Months (N=320)		12 Months (N=292)		Cumulative (N=334)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Corneal edema between 1 week and 1 month after procedure	26	7.8												
Peripheral 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
Epithelium in the interface (epithelial ingrowth; trace/mild)	3	0.9	9	2.7	10	3.9	9	2.7	10	3.1	6	2.1	17	5.1
Diffuse Lamellar Keratitis (DLK, Grade 2 or less)	17[a]	5.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	17[a]	5.1
Foreign body sensation at 1 month or later			38[b]	11.4	26[b]	7.8	17[b]	5.1	14[b]	4.2	8[b]	2.7	68[b]	20.4
Pain at 1 month or later			13[c]	3.9	9[c]	2.7	14[c]	4.2	0	0.0	6[c]	2.1	40[c]	12.0

Note: Shaded areas represent time frames outside complication definition.
[a] All reports of DLK were Grade 1 or less.
[b] Most reports were mild; no marked or severe reports.
[c] Most reports were mild; one moderate report at 3 and 6 months, one marked report at 6 months and at an interim visit.
% = n/N (100)

g) *NEI-RQL-42 Questionnaire*

The National Eye Institute-Refractive Error Quality of Life instrument (NEI-RQL-42) was administered to subjects at the periodic study exams. Results of the NEI-RQL-42 questionnaire assessing binocular subjective visual functioning and well-being yielded positive changes at 6 months vs. preoperative for all questionnaire measures indicating improvements in vision-related wellbeing due to the Advanced CustomVue procedure with iDesign Advanced WaveScan Studio system (**Table 10**). Typical optical visual symptoms reported by LASIK subjects were assessed by the NEI-RQL: improvements in the glare measure, were found at 6 months vs. preoperative with correction. A post-hoc analysis of the individual items comprising the far vision scale is presented in **Table 11**.

The mean scores for “difficulty judging distances”, “difficulty seeing things off to the side”, “difficulty getting used to the dark”, “difficulty driving at night”, and “difficulty driving at night in difficult conditions” all improved at 6 months as compared to preoperative scores with correction.

TABLE 10

Mean Scores of NEI-RQL Questionnaire Measures at 6 Months vs. Preoperative

All Subjects (N=170)

Measure	Preop	6 Months	Change	% Change (Change/Preop)
Clarity of Vision	80.29	91.52	+11.23	14%
Expectations	6.91	76.03	+69.12	1000%
Near Vision	80.59	93.55	+12.97	16%
Far Vision	80.09	92.63	+12.54	16%
Diurnal Fluctuations	79.07	92.30	+13.24	17%
Activity Limitations	63.35	97.87	+34.52	54%
Glare	78.16	84.56	+6.40	8%
Symptoms	83.68	92.25	+8.57	10%
Dependence on Correction	38.14	93.61	+55.35	145%
Worry	42.43	81.18	+38.75	91%
Suboptimal Correction	88.82	98.97	+10.15	11%
Appearance	36.74	91.07	+54.34	148%
Satisfaction with Correction	58.00	92.00	+34.00	59%

Table 11
Mean Scores of Individual Items of the Far Vision Scale of the NEI-RQL Questionnaire
All Myopic Subjects (N=170)

Item	Preop	6 Months	Change	%Change
Difficulty judging distances	85.29	97.65	12.35	14%
Difficulty seeing things off to the side	83.73	97.84	14.12	17%
Difficulty getting used to the dark	76.67	89.02	12.35	16%
Difficulty driving at night	81.03	90.88	9.85	12%
Difficulty driving at night in difficult conditions	73.96	87.72	13.76	19%

Note: Change calculated as 6 months minus preoperative. % Change = Change/Preop

h) *Directed Visual Symptoms*

Table 12 presents subjective visual symptoms at preoperative and 6 months from the "directed symptom assessment" as reported by subjects when specifically queried about each symptom at study visits. The directed symptom assessment questionnaire was not evaluated for its ability to validly assess patient-reported visual symptoms. Reports of subjective visual symptoms were typical following LASIK refractive procedures. Preoperatively, dryness, night glare, halos and difficulty driving at night were reported with the highest severity ("marked" and "severe"). At 6 months, there were no reports of "severe" symptoms and the visual symptoms reported with the highest severity ("marked") included night glare, halos, and difficulty driving at night. However, statistically significant reductions in the proportion of eyes noted with moderate, marked and severe reports of night glare (-5.4%) and difficulty driving at night (-8.7%) were found between preoperative and 6 months (**Table 13**).

TABLE 12

Directed Visual Symptoms at Preoperative and 6 Months

All Eyes (N=334)

		None		Mild		Moderate		Marked		Severe	
Symptom	**Visit**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Pain	Preop	328	98.2%	4	1.2%	2	0.6%	0	0.0%	0	0.0%
	6 Months	320	95.8%	12	3.6%	1	0.3%	1	0.3%	0	0.0%
Tearing	Preop	298	89.2%	34	10.2%	2	0.6%	0	0.0%	0	0.0%
	6 Months	315	94.3%	19	5.7%	0	0.0%	0	0.0%	0	0.0%
Photophobia	Preop	287	85.9%	36	10.8%	11	3.3%	0	0.0%	0	0.0%
	6 Months	282	84.4%	43	12.9%	8	2.4%	1	0.3%	0	0.0%
Foreign Body Sensation	Preop	320	95.8%	14	4.2%	0	0.0%	0	0.0%	0	0.0%
	6 Months	317	94.9%	17	5.1%	0	0.0%	0	0.0%	0	0.0%
Dryness	Preop	195	58.4%	100	29.9%	33	9.9%	6	1.8%	0	0.0%
	6 Months	176	52.7%	130	38.9%	26	7.8%	2	0.6%	0	0.0%
Fluctuation of Vision	Preop	299	89.5%	33	9.9%	2	0.6%	0	0.0%	0	0.0%
	6 Months	281	84.1%	47	14.1%	4	1.2%	2	0.6%	0	0.0%
Day Glare	Preop	287	85.9%	40	12.0%	7	2.1%	0	0.0%	0	0.0%
	6 Months	297	88.9%	30	9.0%	5	1.5%	2	0.6%	0	0.0%
Night Glare	Preop	213	63.8%	83	24.9%	29	8.7%	5	1.5%	4	1.2%
	6 Months	264	79.0%	50	15.0%	14	4.2%	6	1.8%	0	0.0%
Binocular Diplopia	Preop	332	99.4%	2	0.6%	0	0.0%	0	0.0%	0	0.0%
	6 Months	332	99.4%	2	0.6%	0	0.0%	0	0.0%	0	0.0%
Monocular Diplopia	Preop	334	100.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
	6 Months	331	99.1%	3	0.9%	0	0.0%	0	0.0%	0	0.0%
Ghosting	Preop	326	97.6%	8	2.4%	0	0.0%	0	0.0%	0	0.0%
	6 Months	318	95.2%	12	3.6%	4	1.2%	0	0.0%	0	0.0%
Halos	Preop	195	58.4%	100	29.9%	31	9.3%	4	1.2%	4	1.2%
	6 Months	194	58.1%	111	33.2%	22	6.6%	7	2.1%	0	0.0%
Difficulty Driving at Night	Preop	194	58.1%	88	26.3%	46	13.8%	4	1.2%	2	0.6%
	6 Months	259	77.5%	52	15.6%	15	4.5%	8	2.4%	0	0.0%

% = n/N (100)

TABLE 13

Changes in Moderate/Marked/Severe Visual Symptoms at 6 Months vs. Preoperative

All Eyes (N=334)

	Preoperative				6 Months				Difference[a] in Moderate, Marked & Severe Symptoms
	None & Mild		Moderate, Marked & Severe		None & Mild		Moderate, Marked & Severe		
Symptom	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**%**
Pain	332	99.4%	2	0.6%	332	99.4%	2	0.6%	0.0%
Tearing	332	99.4%	2	0.6%	334	100.0%	0	0.0%	-0.6%
Photophobia	323	96.7%	11	3.3%	325	97.3%	9	2.7%	-0.6%
Foreign Body Sensation	334	100.0%	0	0.0%	334	100.0%	0	0.0%	0.0%
Dryness	295	88.3%	39	11.7%	306	91.6%	28	8.4%	-3.3%
Vision Fluctuation	332	99.4%	2	0.6%	328	98.2%	6	1.8%	1.2%
Day Glare	327	97.9%	7	2.1%	327	97.9%	7	2.1%	0.0%
Night Glare	296	88.6%	38	11.4%	314	94.0%	20	6.0%	-5.4%
Binocular Diplopia	334	100.0%	0	0.0%	334	100.0%	0	0.0%	0.0%
Monocular Diplopia	334	100.0%	0	0.0%	334	100.0%	0	0.0%	0.0%
Ghosting	334	100.0%	0	0.0%	330	98.8%	4	1.2%	1.2%
Halos	295	88.3%	39	11.7%	305	91.3%	29	8.7%	-3.0%
Driving at night	282	84.4%	52	15.6%	311	93.1%	23	6.9%	-8.7%

[a] Difference = 6 months minus preoperative

% = n/N (100)

i) *Contrast Sensitivity*

Monocular best corrected distance contrast sensitivity was evaluated preoperatively and postoperatively at 3, 6 and 12 months under mesopic (3 cd/m^2) conditions with and without glare and photopic (85 cd/m^2) conditions without glare at 4 spatial frequencies (3, 6, 12, and 18 cycles per degree, cpd). As shown in **Table 14**, mean statistically significant (**p<0.0001**) improvements in contrast sensitivity of up to 0.15 log units or more at 6 months from preoperative were found under mesopic conditions with and without glare at 3 spatial frequencies (6, 12 and 18 cpd). There were no substantial changes in mean contrast sensitivity under photopic conditions without glare. **Table 15** presents the number of eyes unable to see the reference patterns at each spatial frequency and lighting condition at preoperative and 6 months. At 6 months, fewer eyes (up to 6.0%) were unable to see the reference pattern scores for all spatial frequencies and lighting conditions compared to preoperatively (up to 14%). As shown in **Table 16**, most eyes (≥89%) had no change or clinically significant improvements in contrast sensitivity (0.30 log units or more) under all lighting conditions at 6 months vs. preoperative. Under mesopic conditions with or without glare, there was a four-fold increase in the proportions of eyes with clinically significant increases (41%-47%) compared to decreases (≤11%). Overall, contrast sensitivity results were excellent with statistically

significant improvements in mean contrast sensitivity compared to preoperative under mesopic conditions, and most eyes experiencing either no change or an improvement in contrast sensitivity postoperatively compared to preoperatively.

TABLE 14

Mean Change in Contrast Sensitivity at 6 Months From Preoperative

All Eyes (N=334)

	Mean Change			
Lighting Condition	**3 cpd**	**6 cpd**	**12 cpd**	**18 cpd**
Photopic Without Glare				
Mean (Log units)	-0.01	0.02	0.08	0.06
Standard error	0.011	0.015	0.019	0.018
Adjusted P-value	0.618	0.618	**<0.0001**	**0.0008**
Mesopic With Glare				
Mean (Log units)	0.04	0.16	0.23	0.22
Standard error	0.015	0.019	0.024	0.024
Adjusted P-Value	**0.045**	**<0.0001**	**<0.0001**	**<0.0001**
Mesopic Without Glare				
Mean (Log units)	0.07	0.17	0.22	0.24
Standard error	0.015	0.022	0.026	0.024
Adjusted P-Value	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**

Note: Positive values for "change from preoperative" represent increase in contrast sensitivity scores.

Note: Data for eyes that were unable to see the reference pattern were imputed; means < standard errors are > calculated values.

Note: P-values are based on one-sample t-test and adjusted for multiplicity using the Bonferroni step-down method.

TABLE 15

Proportions of Eyes Unable to See the Contrast Sensitivity Reference Patterns at Preoperative and 6 Months

All Eyes (N=334)

Lighting Condition	Spatial Frequency	Preoperative n	Preoperative %	6 Months n	6 Months %
Photopic without Glare	3.0 cpd	2	0.6%	0	0.0%
	6.0 cpd	5	1.5%	2	0.6%
	12.0 cpd	12	3.6%	9	2.7%
	18.0 cpd	9	2.7%	7	2.1%
Mesopic without Glare	3.0 cpd	4	1.2%	0	0.0%
	6.0 cpd	15	4.5%	3	0.9%
	12.0 cpd	38	11.4%	12	3.6%
	18.0 cpd	34	10.2%	18	5.4%
Mesopic with Glare	3.0 cpd	7	2.1%	0	0.0%
	6.0 cpd	29	8.7%	10	3.0%
	12.0 cpd	40	12.0%	20	6.0%
	18.0 cpd	46	13.8%	14	4.2%

%=n/N(100)

TABLE 16

Clinically Significant Changes[a] in Contrast Sensitivity at 6 Months from Preoperative

All Eyes (N=334)

Lighting Condition	Decrease n	Decrease %	No change n	No change %	Increase n	Increase %
Photopic without Glare	36	10.8%	234	70.1%	64	19.2%
Mesopic without Glare	32	9.6%	164	49.1%	138	41.3%
Mesopic with Glare	36	10.8%	142	42.5%	156	46.7%

[a] A difference of ≥ 0.30 log units from preoperative at 2 or more spatial frequencies is considered a clinically significant change in contrast sensitivity.

% = n/N(100)

a) *Higher Order Aberrations*

Analyses of higher order aberrations (HOA) showed that HOA root mean square (RMS; absolute value) increased postoperatively, mostly associated with an increase in coma. All other higher order aberration terms, on average, increased by no more than 0.01 µm with 4 mm standardized wavefront diameters and no more than 0.03 µm with 5 mm standardized wavefront diameters (**Table 17**).

TABLE 17
Higher Order Aberrations (HOA) RMS (µm) at Preoperative and 6 Months
All Myopic Eyes

	4 mm Standardized Wavefront Diameters		5 mm Standardized Wavefront Diameters	
	Preoperative (n=334)	**6 Months (n=310)**	**Preoperative (n=316)**	**6 Months (n=290)**
	Mean+/-SD	**Mean+/-SD**	**Mean+/-SD**	**Mean+/-SD**
HOA RMS (µm)	0.09 +/- 0.04	0.13 +/- 0.07	0.17 +/- 0.07	0.24 +/- 0.11
Coma	0.06 +/- 0.04	0.09 +/- 0.06	0.10 +/- 0.07	0.16 +/- 0.11
Spherical Aberration	0.02 +/- 0.02	0.03 +/- 0.03	0.06 +/- 0.04	0.07 +/- 0.05
Trefoil	0.05 +/- 0.03	0.06 +/- 0.04	0.09 +/- 0.05	0.09 +/- 0.06
Secondary Coma	0.00 +/- 0.00	0.01 +/- 0.01	0.01 +/- 0.01	0.03 +/- 0.02
Secondary Astigmatism	0.02 +/- 0.01	0.03 +/- 0.02	0.04 +/- 0.02	0.06 +/- 0.05
Secondary Spherical Aberration	0.00 +/- 0.00	0.01 +/- 0.00	0.01 +/- 0.01	0.02 +/- 0.02
Fifth Order	0.01 +/- 0.01	0.01 +/- 0.01	0.02 +/- 0.01	0.04 +/- 0.02
Sixth Order	0.00 +/- 0.00	0.01 +/- 0.01	0.01 +/- 0.01	0.03 +/- 0.02
Spherical Aberration Signed	0.02 +/- 0.03	0.00 +/- 0.04	0.04 +/- 0.06	0.04/- 0.08

ii Effectiveness Results

A summary of the key effectiveness variables over time is presented in **Table 18** for all myopic eyes.

a) *85% of eyes with a UCVA of 20/40 or better:* At 6 months, UCVA of 20/40 or better was achieved in 98.2% (328/334) of eyes, exceeding the primary study effectiveness endpoint target of 85% of eyes with 20/40 or better UCVA. Additionally, the lower 95% confidence interval (96.1%) exceeded the target value as well. Furthermore at 6 months, 82.6% (276/334) of eyes were 20/20 or better and 61.7% (206/334) were 20/16 or better. Overall, the proportions of eyes that achieved UCVA of 20/40 or better exceeded the target rate (85%) across all postoperative study visits.

b) *Proportion of eyes of eyes with an MRSE within 0.50 D and 1.00 D of intended correction:* The secondary effectiveness endpoints pertaining to the accuracy of treatment were met at 6 months with 68.9% (230/334) of eyes having MRSE within 0.50 D of emmetropia and 93.4% (312/334) within 1.00 D, exceeding the study endpoint targets of 50% within 0.50 D and 75% within 1.00 D. Additionally at 6 months, almost all eyes (99.4%; 332/334) had MRSE within 2.00 D; two eyes (0.6%; 2/334) of the same subject were under-corrected by >2.00 D (MRSE of -2.50 D each).

TABLE 18

Key Effectiveness Variables Over Time

All Eyes (N=334)

Effectiveness Variable	1 Month (n=334) n % (95% CI)	3 Months (n=334) n % (95% CI)	6 Months (n=334) n % (95% CI)	9 Months (n=320) n % (95% CI)	12 Months (n=290) n % (95% CI)
UCVA 20/16 or better	215 64.4% (59.0, 69.5)	208 62.3% (56.8, 67.5)	206 61.7% (56.2, 66.9)	202 63.1% (57.6, 68.4)	178 61.4% (55.5, 67.0)
UCVA 20/20 or better	294 88% (84.1, 91.3)	283 84.7% (80.4, 88.4)	276 82.6% (78.1, 86.5)	268 83.8% (79.2, 87.6)	231 79.7% (74.6, 84.1)
UCVA 20/40 or better[a]	332 99.4% (97.9, 99.9)	332 99.4% (97.9, 99.9)	328 98.2% (96.1, 99.3)	313 97.8% (95.5, 99.1)	280 96.6% (93.8, 98.3)
MRSE +/- 0.50 D[b]	261 78.1% (73.3, 82.5)	240 71.9% (66.7, 76.6)	230 68.9% (63.6, 73.8)	209 65.3% (59.8, 70.5)	191 65.9% (60.1, 71.3)
MRSE +/- 1.00 D[c]	326 97.6% (95.3, 99.0)	314 94% (90.9, 96.3)	312 93.4% (90.2, 95.8)	288 90% (86.2, 93.1)	265 91.4% (87.5, 94.3)
MRSE +/- 2.00 D	334 100% (99.1, 100)	332 99.4% (97.9, 99.9)	332 99.4% (97.9, 99.9)	318 99.4% (97.8, 99.9)	289 99.7% (98.1, 100)

Note: Confidence Intervals calculated based on Clopper-Pearson Exact method.

[a] **Study endpoint target**: 85% of eyes 20/40 or better UCVA
[b] **Study endpoint target:** 50% of eyes within 0.50 D MRSE
[c] **Study endpoint target**: 75% of eyes within 1.00 D MRSE'
% = n/N(100)

The key effectiveness variables at 6 months stratified by preoperative IDSE are presented in **Table 19**. All preoperative IDSE groups either achieved or were not statistically

significantly different from the effectiveness study targets for UCVA 20/40 or better (target 85%) and MRSE within 0.50 D (target 50%) and MRSE within 1.00 D (target 75%).

TABLE 19

Key UCVA and MRSE Variables at 6 Months by Preop *iDesign AWS* Spherical Equivalent (IDSE)

All Eyes (N=334)

Preoperative IDSE Diopter Group (n)	UCVA 20/20 or better n % (95% CI)	UCVA 20/40 or better[a] n % (95% CI)	MRSE within 0.50 D[b] n % (95% CI)	MRSE within 1.00 D[c] n % (95% CI)
< -1 to ≥ -2 D (n=22)	17 77.3% (54.6, 92.2)	22 100% (87.3, 100)	12 54.5% (32.2, 75.6)	20 90.9% (70.8, 98.9)
< -2 to ≥ -3 D (n=27)	26 96.3% (81.0, 99.9)	27 100% (89.5, 100)	19 70.4% (49.8, 86.2)	26 96.3% (81.0, 99.9)
< -3 to ≥ -4 D (n=40)	32 80.0% (64.4, 90.9)	40 100% (92.8, 100)	29 72.5% (56.1, 85.4)	40 100% (92.8, 100)
< -4 to ≥ -5 D (n=42)	38 90.5% (77.4, 97.3)	42 100% (93.1, 100)	33 78.6% (63.2, 89.7)	42 100% (93.1, 100)
<- 5 to ≥ -6 D (n=43)	40 93.0% (80.9, 98.5)	43 100% (93.3, 100)	39 90.7% (77.9, 97.4)	43 100% (93.3, 100)
< -6 to ≥ -7 D (n=36)	29 80.6% (64.0, 91.8)	34 94.4% (81.3, 99.3)	20 55.6% (38.1, 72.1)	30 83.3% (67.2, 93.6)
< -7 to ≥ -8 D (n=31)	23 74.2% (55.4, 88.1)	30 96.8% (83.3, 99.9)	19 61.3% (42.2, 78.2)	26 83.9% (66.3, 94.5)
< -8 to ≥ -9 D (n=31)	26 83.9% (66.3, 94.5)	31 100% (90.8, 100)	24 77.4% (58.9, 90.4)	30 96.8% (83.3, 99.9)
< -9 to ≥ -10 D (n=23)	20 87.0% (66.4, 97.2)	22 95.7% (78.1, 99.9)	17 73.9% (51.6, 89.8)	21 91.3% (72.0, 98.9)
< -10 to ≥ -11 D (n=24)	16 66.7% (44.7, 84.4)	22 91.7% (73.0, 99.0)	10 41.7%[d] (22.1, 63.4)	20 83.3% (62.6, 95.3)
< -11 to ≥ -12 D (n=15)	9 60.0% (32.3, 83.7)	15 100% (81.9, 100)	8 53.3% (26.6, 78.7)	14 93.3% (68.1, 99.8)
Total (N=334)	276 82.6% (78.1, 86.5)	328 98.2% (96.1, 99.3)	230 68.9% (63.6, 73.8)	312 93.4% (90.2, 95.8)

Note: Confidence Intervals calculated based on Clopper-Pearson Exact method.

[a] Study endpoint target: 85% of eyes 20/40 or better UCVA
[b] Study endpoint target: 50% of eyes within 0.50 D MRSE
[c] Study endpoint target: 75% of eyes within 1.00 D MRSE
[d] Not statistically significantly different from target (50%); one of the eyes that was under-corrected by >2.00 D MRSE at 6 months is in this diopter group.
% = n/N(100)

The key effectiveness variables at 6 months stratified by preoperative IDC are presented in **Table 20.** UCVA and MRSE effectiveness endpoints were met for all preoperative

IDC groups with ≥97.3% of eyes achieving UCVA of 20/40 or better (target 85%), ≥53.3% of eyes achieving MRSE within 0.50 D (target 50%), and ≥90.0% of eyes achieving MRSE within 1.00 D (target 75%).

TABLE 20

Key UCVA and MRSE Variables at 6 Months by Preoperative *iDesign AWS* Cylinder (IDC)

All Eyes (N=334)

Preoperative IDC Diopter Group (n)	UCVA 20/20 or better n % (95% CI)	UCVA 20/40 or better[a] n % (95% CI)	MRSE within 0.50 D[b] n % (95% CI)	MRSE within 1.00 D[c] n % (95% CI)
0 to -1 D (n=150)	123 82.0% (74.9, 87.8)	146 97.3% (93.3, 99.3)	99 66.0% (57.8, 73.5)	138 92.0% (86.4, 95.8)
<-1 to -2 D (n=60)	49 81.7% (69.6, 90.5)	59 98.3% (91.1, 100)	32 53.3% (40.0, 66.3)	54 90.0% (79.5, 96.2)
<-2 to -3 D (n=47)	42 89.4% (76.9, 96.5)	46 97.9% (88.7, 99.9)	39 83.0% (69.2, 92.4)	45 95.7% (85.5, 99.5)
<-3 to -4 D (n=34)	27 79.4% (62.1, 91.3)	34 100% (91.6, 100)	26 76.5% (58.8, 89.3)	34 100% (91.6, 100)
<-4 to -5 D (n=26)	22 84.6% (65.1, 95.6)	26 100% (89.1, 100)	19 73.1% (52.2, 88.4)	25 96.2% (80.4, 99.9)
<-5 to -6 D (n=10)	6 60.0% (26.2, 87.8)	10 100% (74.1, 100)	8 80.0% (44.4, 97.5)	9 90.0% (55.5, 99.7)
<-6 to -7 D (n=5)	5 100% (54.9, 100)	5 100% (54.9, 100)	5 100% (54.9, 100)	5 100% (54.9, 100)
<-7 to -8 D (n=2)	2 100% (22.4, 100)	2 100% (22.4, 100)	2 100% (22.4, 100)	2 100% (22.4, 100)
Total (N=334)	276 82.6% (78.1, 86.5)	328 98.2% (96.1, 99.3)	230 68.9% (63.6, 73.8)	312 93.4% (90.2, 95.8)

Note: Confidence Intervals calculated based on Clopper-Pearson Exact method.

[a] Study endpoint target: 85% of eyes 20/40 or better UCVA
[b] Study endpoint target: 50% of eyes within 0.50 D MRSE
[c] Study endpoint target: 75% of eyes within 1.00 D MRSE
% = n/N(100)

c) *UCVA*: **Table 21** presents the distribution of UCVA results over time for all myopic eyes. Again, the proportions of eyes that achieved UCVA of 20/40 or better (≥96.6%) exceeded the target rate (85%) across postoperative study visits. The majority (≥61%) of eyes achieved 20/16 or better UCVA across all postoperative study visits.

TABLE 21

UCVA Over Time

All Eyes (N=334)

Acuity	1 Month (n=334) n	%	3 Month (n=334) n	%	6 Month (n=334) n	%	9 Month (n=320) n	%	12 Month (n=290) n	%
20/10 or better	8	2.4%	10	3.0%	8	2.4%	10	3.1%	9	3.1%
20/12.5 or better	70	21.0%	81	24.3%	70	21.0%	68	21.3%	62	21.4%
20/16 or better	215	64.4%	208	62.3%	206	61.7%	202	63.1%	178	61.4%
20/20 or better	294	88.0%	283	84.7%	276	82.6%	268	83.8%	231	79.7%
20/25 or better	323	96.7%	315	94.3%	311	93.1%	291	90.9%	263	90.7%
20/32 or better	331	99.1%	330	98.8%	325	97.3%	304	95.0%	277	95.5%
20/40 or better	332	99.4%	332	99.4%	328	98.2%	313	97.8%	280	96.6%
20/50 or better	334	100%	332	99.4%	330	98.8%	315	98.4%	288	99.3%
20/63 or better	334	100%	332	99.4%	330	98.8%	317	99.1%	289	99.7%
20/80 or better	334	100%	332	99.4%	331	99.1%	317	99.1%	290	100%
20/100 or better	334	100%	333	99.7%	334	100%	320	100%	290	100%
Worse than 20/100	0	0.0%	1	0.3%	0	0.0%	0	0.0%	0	0.0%

% = n/N (100)

Table 22 presents the differences in postoperative UCVA achieved compared to preoperative best spectacle corrected visual acuity (BSCVA) for all myopic eyes. At 6 months, 67.1% (224/334) of eyes achieved the same or better acuity level postoperatively without correction as preoperatively with correction.

TABLE 22

Postoperative UCVA Compared to Preoperative BSCVA

All Eyes (N=334)

Acuity	1 Month n	1 Month %	3 Month n	3 Month %	6 Month n	6 Month %	9 Month n	9 Month %	12 Month n	12 Month %
>2 lines better	0	0.0%	1	0.3%	0	0.0%	1	0.3%	0	0.0%
2 lines better	8	2.4%	11	3.3%	11	3.3%	13	4.1%	6	2.1%
1 line better	86	25.7%	94	28.1%	88	26.3%	76	23.8%	82	28.3%
Equal	154	46.1%	128	38.3%	125	37.4%	133	41.6%	102	35.2%
1 line worse	59	17.7%	65	19.5%	71	21.3%	57	17.8%	53	18.3%
2 lines worse	16	4.8%	17	5.1%	16	4.8%	13	4.1%	18	6.2%
>2 lines worse	11	3.3%	18	5.4%	23	6.9%	27	8.4%	29	10.0%
All	334	100%	334	100%	334	100%	320	100%	290	100%

%= n/N(100)

d) *Refractive Stability*

95% of eyes achieve refractive stability: Refractive stability was achieved at the 6-month study visit based on analyses performed using both a consecutive cohort (eyes with data at for at least two consecutive study visits) and a consistent cohort (eyes with data at all periodic study exams). Results were similar between the two cohorts and the criteria for determining refractive stability for both MRSE and MRC were met at 6 months in both cohorts. As shown in **Table 23**, at least 99% of eyes had ≤1.00 D of change in MRSE (≥99.1%) and MRC (≥99.3%) between any two visits, meeting the criterion of >95% of eyes with ≤1.00 D of change in MRSE and MRC. The mean rate of change was -0.01 D/month for both MRSE and MRC between 3 and 6 months meeting the criterion of ≤0.04 D/month. The rate of change in MRSE and MRC decreased monotonically over time with the 95% confidence intervals including zero, and refractive stability was confirmed at 9 months with a large sample size.

TABLE 23

MRSE and Manifest Refractive Cylinder (MRC) Stability

All Eyes - Consecutive Cohort

Distributions	Between 1 and 3 Months (N=334) n % (95% CI)	Between 3 and 6 Months (N=334) n % (95% CI)	Between 6 and 9 Months (N=320) n % (95% CI)	Between 9 and 12 Months (N=284) n % (95% CI)
Change in MRSE by ≤1.0 D[a]	332 99.4% (97.9, 99.9)	331 99.1% (97.4, 99.8)	319 99.7% (98.3, 100)	282 99.3% (97.5, 99.9)
Change in MRC by ≤1.0 D[a]	332 99.4% (97.9, 99.9)	332 99.4% (97.9, 99.9)	319 99.7% (98.3, 100)	284 100% (99.0, 100)
Mean Outcomes	**D +/- SD (95% CI)**	**D +/- SD (95% CI)**	**D +/- SD (95% CI)**	**D +/- SD (95% CI)**
Mean Change in MRSE	-0.096 +/- 0.293 (-0.128, -0.064)	-0.030 +/- 0.321 (-0.064, 0.005)	-0.024 +/- 0.288 (-0.056, 0.007)	-0.033 +/- 0.297 (-0.068, 0.001)
Mean Change in MRSE per Month[b]	-0.048	-0.010	-0.008	-0.011
Mean Change in MRC	-0.019 +/- 0.269 (-0.048, 0.010)	-0.026 +/- 0.287 (-0.057, 0.005)	-0.007 +/- 0.284 (-0.038, 0.024)	0.006 +/- 0.245 (-0.022, 0.035)
Mean Change in MRC per Month[b]	-0.009	-0.009	-0.002	0.002

Note: Confidence Intervals calculated based on Clopper-Pearson Exact method.

[a] Refractive stability criterion: 95% of eyes with change of ≤1.00 D between visits
[b] Refractive stability criterion: mean change of ≤0.04 D/month between visits

e) *Manifest Refractive Outcomes Descriptive Statistics*: Mean manifest refractive outcomes over time are presented in **Table 24**. At 6 months, mean MRSE was -0.46 D (SD 0.42 D), demonstrating a consistent under-correction.

TABLE 24

Mean Refractive Outcomes Over Time All Eyes

Variable	Preoperative N=334	1 Month N=334	3 Month N=334	6 Month N=334	9 Month N=320	12 Month N=290
MRSE (D) +/- SD	-6.21 +/- 2.78	-0.33 +/- 0.35	-0.43 +/- 0.39	-0.46 +/- 0.42	-0.49 +/- 0.45	-0.49 +/- 0.40
MRS (D) +/-SD	-5.32 +/- 2.97	-0.19 +/- 0.39	-0.28 +/- 0.42	-0.29 +/- 0.45	-0.33 +/- 0.46	-0.33 +/- 0.41
MRC (D) +/- SD	-1.77 +/- 1.65	-0.28 +/- 0.34	-0.30 +/- 0.35	-0.33 +/- 0.36	-0.33 +/- 0.36	-0.33 +/- 0.32

MRSE = manifest refraction spherical equivalent, MRS = manifest refractive sphere, MRC = manifest refractive cylinder

f) *Additional Cylinder Correction Analyses:* **Table 25** presents the proportions of eyes with residual manifest cylinder magnitude at 6 months and the absolute shift in axis from preoperative. At 6 months, an axis shift of >30° from preoperative was noted for 18.6% (46/247) of eyes; however, only two (4.3%; 2/46) of these eyes (with axis change of 69˚and 70˚) had a residual cylinder magnitude >0.50 D. Both of these eyes achieved UCVA of 20/25 or better. In addition, two eyes (0.8%; 2/247) had >2.0 D of residual MRC at 6 months with axis changes of >15° to ≤30° (21˚and 30˚) vs. preoperative. Both of these eyes achieved UCVA of 20/32.

TABLE 25

Residual Astigmatic Axis Error (Non-Vector) at 6 Months

Eyes with Preoperative Myopic Astigmatism (N=247)

	Absolute Shift in Axis						
Residual Manifest Cylinder Magnitude	**0° (N=84) n % (95% CI)**	**≤5° (N=36) n % (95% CI)**	**>5° to ≤10° (N=19) n % (95% CI)**	**>10° to ≤15° (N=21) n % (95% CI)**	**>15° to ≤30° (N=41) n % (95% CI)**	**>30° (N=46) n % (95% CI)**	**Total (N=247) n % (95% CI)**
0.0 D	78 92.9% (85.1, 97.3)	0 0.0% (- , -)	0 0.0% (- , -)	0 0.0% (- , -)	0 0.0% (- , -)	0 0.0% (- , -)	78 31.6% (25.8, 37.8)
>0 to ≤0.5 D	6 7.1% (2.7, 14.9)	24 66.7% (49.0, 81.4)	14 73.7% (48.8, 90.9)	15 71.4% (47.8, 88.7)	31 75.6% (59.7, 87.6)	44 95.7% (85.2, 99.5)	134 54.3% (47.8, 60.6)
>0.5 to ≤1.0 D	0 0.0% (- , -)	7 19.4% (8.2, 36.0)	4 21.1% (6.1, 45.6)	4 19.0% (5.4, 41.9)	6 14.6% (5.6, 29.2)	2 4.3% (0.5, 14.8)	23 9.3% (6.0, 13.6)
>1.0 to ≤2.0 D	0 0.0% (- , -)	5 13.9% (4.7, 29.5)	1 5.3% (0.1, 26.0)	2 9.5% (1.2, 30.4)	2 4.9% (0.6, 16.5)	0 0.0% (- , -)	10 4.0% (2.0, 7.3)
>2.0 to ≤3.0 D	0 0.0% (- , -)	0 0.0% (- , -)	0 0.0% (- , -)	0 0.0% (- , -)	2 4.9% (0.6, 16.5)	0 0.0% (- , -)	2 0.8% (0.1, 2.9)
Total	**84 100%**	**36 100%**	**19 100%**	**21 100%**	**41 100%**	**46 100%**	**247 100%**

Note: Confidence Intervals calculated based on C lopper-Pearson Exact method.

Vector analysis summary statistics at 6 months are presented in **Table 26** for eyes with preoperative manifest refractive astigmatism of >0.50 D. At 6 months, the mean absolute error vector (EV) magnitude was less than 0.50 D (0.36 D; SD 0.36 D), the mean correction ratio (CR) was close to 1.0 (0.94; SD 0.18) and the mean error ratio (ER) was close to zero (0.19; SD 0.20).

TABLE 26

Vector Analysis Summary at 6 Months

Eyes with Preoperative Manifest Myopic Astigmatism[a] (N=221)

Preoperative Cylinder magnitude	n	|IRC| (Mean+/-SD)	|SIRC| (Mean+/-SD)	|EV| (Mean+/-SD)	CR (Mean+/-SD)	ER (Mean+/-SD)
All	221	2.51 +/- 1.58	2.32 +/- 1.49	0.36 +/- 0.36	0.94 +/- 0.18	0.19 +/- 0.20
>0.5 to ≤1.0 D	54	0.86 +/- 0.13	0.81 +/- 0.25	0.30 +/- 0.23	0.95 +/- 0.29	0.36 +/- 0.28
>1.0 to ≤2.0 D	54	1.61 +/- 0.31	1.57 +/- 0.39	0.23 +/- 0.22	0.98 +/- 0.17	0.14 +/- 0.15
>2.0 to ≤3.0 D	44	2.54 +/- 0.26	2.31 +/- 0.38	0.34 +/- 0.30	0.91 +/- 0.11	0.13 +/- 0.12
>3.0 to ≤4.0 D	30	3.57 +/- 0.29	3.29 +/- 0.49	0.44 +/- 0.38	0.92 +/- 0.13	0.12 +/- 0.11
>4.0 to ≤5.0 D	22	4.47 +/- 0.26	3.96 +/- 0.45	0.59 +/- 0.45	0.89 +/- 0.10	0.13 +/- 0.10
>5.0 to ≤6.0 D	10	5.55 +/- 0.31	5.06 +/- 0.75	0.75 +/- 0.75	0.91 +/- 0.11	0.14 +/- 0.14
>6.0 to ≤7.0 D	4	6.63 +/- 0.32	6.30 +/- 0.85	0.38 +/- 0.60	0.95 +/- 0.09	0.06 +/- 0.10
>7.0 to ≤8.0 D	3	7.33 +/- 0.14	7.18 +/- 0.11	0.25 +/- 0.00	0.98 +/- 0.02	0.03 +/- 0.00

[a] Eyes with preoperative manifest refractive cylinder (MRC) magnitude >0.50 D
IRC = Intended refractive correction
SIRC = Surgically induced refractive correction
EV = Error vector magnitude
CR = Correction Ratio (SIRC/IRC)
ER = Error ratio (EV/IRC)

iii. Factors Associated with Outcomes

Covariate analyses were performed for preoperative differences among sites (race, age, and iDesign Advanced WaveScan Studio system refractions) and factors found to be associated with primary effectiveness outcomes (gender, race, contact lens wear, preoperative IDSE, IDS and IDC, site, surgeon, iris registration use and myopic group [low: preoperative IDSE ≥-6 D; high: preoperative IDSE <-6 D to ≥-12 D]). When controlling for site, race, age and preoperative iDesign Advanced WaveScan Studio system refractions were not found to have effects on outcomes, indicating that data from all sites are poolable. Additionally, covariate analyses of significant factors showed no site interactions and that iris registration use, contact lens wear and myopic group (low/high) had effects on outcomes for accuracy of MRSE. However, all outcomes stratification results met or exceeded study targets based on the factors evaluated.

Device Failures and Replacements

There were no laser failures or replacements during the course of this study. There were four (4) iDesign Advanced WaveScan Studio system failures during the course of this study. None of these replaced units impacted patient outcomes or were associated with adverse events. Two iDesign Advanced WaveScan Studio systems were replaced due to software issue or hardware malfunction/failure isolated to the specific device. The hardware related failure included a faulty USB port. The second failure was due to the installed software that was not enabled. The third return was due to user dissatisfaction with the Hartman-Shack display screen on the device. Lastly, a fourth return was for root cause analysis of a user workflow issue. The third

and fourth returns were not related to a device failure or malfunction.

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 14 investigators of which none were full-time or part-time employees of the sponsor and four had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: None (0) of the investigators
- Significant payment of other sorts: Four (4) of the investigators
- Proprietary interest in the product tested held by the investigator: : None (0) of the investigators
- Significant equity interest held by investigator in sponsor of covered study: None (0) of the investigators

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

Several prior clinical investigations on myopic LASIK correction using the iDesign Advanced WaveScan Studio system were conducted. An AMO-sponsored, prospective clinical investigation was conducted in Canada in 2011 under an Investigational Testing Authorization to evaluate performance and acceptability of LASIK treatment using the iDesign Advanced WaveScan Studio System. Results of 143 myopic eyes through 6 months were evaluated. Device performance was found acceptable and results exceeded effectiveness and safety targets. Based on results of the Canadian study, an algorithm adjustment was determined and implemented in the U.S. IDE clinical study. Two investigator-initiated, retrospective studies of myopic LASIK treatment using the iDesign Advanced WaveScan Studio System were performed in the UK[(1,2)]. These studies used the same algorithm adjustment as the U.S. IDE clinical study. A total of 864 eyes were evaluated between the two studies: 243 eyes in one study were followed through 1 month and 621 eyes in the other study were followed through 3 months. Based on results in both studies, it was concluded that wavefront-guided LASIK using the iDesign Advanced WaveScan Studio System for the treatment of myopia was effective, safe and predictable in the early postoperative time period.

XII. PANEL RECOMMENDATIONS

In accordance with the provisions of section 5159C)(3) of the act as amended by the Safe Medical Device Act of 1990, this PMA was not referred to the Ophthalmic Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

In the clinical investigation of wavefront-guided LASIK correction of myopic refractive errors with the iDesign Advanced WaveScan Studio System and STAR S4 IR Excimer Laser System, effectiveness outcomes were found to exceed study targets. Refractive stability was achieved at 6 months; at this time, the proportion of eyes with a UCVA of 20/40 or better (Target 85%; iDesign AWS 98.2%), and the proportions of eyes that achieve MRSE within 0.50 D (Target 50%; iDesign AWS 68.9%) and 1.00 D (Target 75%; iDesign AWS 93.4%) exceeded the target values. Evaluating intended vs. achieved and mean MRSE outcomes at 6 months showed a consistent under-correction indicating that an algorithm adjustment should provide refractive outcomes closer to emmetropia; nevertheless, the accuracy of treatment in this study exceeded endpoint targets and all criteria for effectiveness were met.

B. Safety Conclusions

In the clinical investigation of wavefront-guided LASIK correction of myopic refractive errors with the iDesign Advanced WaveScan Studio System and STAR S4 IR Excimer Laser System, safety outcomes were found to be acceptable and met the safety targets. At

6 months, the proportion of eyes with >2 line loss of BSCVA (Target <5%; iDesign AWS 0.0%), the proportion of eyes with BSCVA worse than 20/40 (Target <1%; iDesign AWS 0%), the proportion of eyes with induced manifest refractive astigmatism >2.00 D (Target <5%; iDesign AWS 0.3%), and the rate of serious, ocular adverse events (Target <1%; iDesign AWS 1.2%; p=0.7166 vs. 1%) were within or not statistically different from target values. Additionally, rates of typical LASIK-related complications and adverse events were low. Statistically significant improvements in mesopic contrast sensitivity with and without glare were found at 6 months. Subjective symptoms were typical following LASIK refractive procedures. Additionally, using the NEI-RQL-42 questionnaire, improvements in vision-related wellbeing and visual functioning, including improvements in glare, were found at 6 months following LASIK correction of myopia with the iDesign Advanced WaveScan Studio system and STAR S4 IR Excimer Laser system.

C. Benefit-Risk Conclusions

All effectiveness study endpoint targets were exceeded with 82.6% achieving 20/20 or better uncorrected visual acuity postoperatively compared to 0.0% preoperatively. The primary effectiveness endpoint of UCVA of 20/40 or better was achieved at 6 months in 98.2% (328/334) of eyes, exceeding the study endpoint target of 85% of eyes with 20/40 or better UCVA. At 6 months, 67.1% (224/334) of eyes achieved the same or better acuity level postoperatively without correction as preoperatively with correction.

The secondary effectiveness endpoints pertaining to the accuracy of treatment were met at 6 months with 68.9% of all eyes having MRSE within 0.50 D of emmetropia and 93.4% within 1.00 D, exceeding the study endpoint targets of 50% within 0.50 D and 75% within 1.00 D. At 6 months, 68.9% of eyes had manifest refraction spherical equivalent (MRSE) within 0.50 D of emmetropia and 93.4% were within 1.00 D, exceeding the study endpoint targets of 50% within 0.50 D and 75% within 1.00 D. At 6 months, 88.6% of eyes were within 0.50 D and 95.8% were within 1.00 D of zero cylinder. Mean MRC at 6 months was -0.33 D (SD 0.36 D). Based on cylinder, the accuracy of treatment was 81.6% at 6 months for all eyes.

At 6 months, 100% of eyes had BSCVA of 20/20 or better. No eyes had BSCVA worse than 20/40 postoperatively at any time during the study. No eyes had a decrease in BSCVA of >2 lines at 6 months vs. preoperative, meeting the primary endpoint safety target of <5% of eyes with a loss of >2 lines of BSCVA. No eyes had preoperative BSCVA of 20/20 or better but worse than 20/40 postoperatively at any time during the study, meeting the safety endpoint target of <1% of eyes with preoperative BSCVA of 20/20 or better having BSCVA worse than 20/40 postoperatively. One eye (0.3%) had induced manifest refractive astigmatism >2.00 D at 6 months, meeting the safety criterion of <5% of eyes with induced manifest refractive astigmatism >2.00 D. Complication and adverse event rates in this study were low.

Sufficient clinical data are available to support the conclusion that the benefits of the Advanced CustomVue Treatment using iDesign Advanced WaveScan Studio outweigh

the risks for patients within the entire treatment range studied in the IDE. Available clinical study data demonstrate similar effectiveness and no substantial increased safety risks for any subgroups, such as higher refractive error, as compared to the entire study population.

Overall, based on the clinical trial results and published literature, there is reasonable assurance of the safety and effectiveness of wavefront-guided LASIK correction of myopic refractive errors for the proposed indication using the iDesign Advanced WaveScan Studio System and Star S4 IR Excimer Laser System.

D. Overall Conclusions

Results of the pre-clinical and clinical investigation demonstrate the safety and effectiveness of wavefront-guided LASIK correction of myopic refractive errors with the iDesign Advanced WaveScan Studio System and STAR S4 IR Excimer Laser System. All effectiveness endpoint targets at 6 months were exceeded demonstrating the ability of the iDesign Advanced WaveScan Studio system in conjunction with the STAR S4 IR Excimer Laser to provide good uncorrected visual acuity with accurate and stable refractive outcomes. Additionally, all safety endpoint targets were achieved at 6 months with low rates of adverse events, no loss of BSCVA >2 lines or BSCVA worse than 20/40, minimal induced manifest refractive astigmatism >2.00 D, increased mesopic contrast sensitivity, increased subjective vision-related wellbeing and visual functioning, including improvements in glare. Based on these results, there is reasonable assurance of the safety and effectiveness of wavefront-guided LASIK correction of myopic refractive errors for the proposed indication using the iDesign Advanced WaveScan Studio System and STAR S4 IR Excimer Laser System.

XIV. CDRH DECISION

CDRH issued an approval order on May 6, 2015

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

XV. 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.

Post-approval Requirement and Restrictions: See approval order.

XVI. REFERENCES

1. Schallhorn S; Brown M; Venter J, Teenan D, Hettinger K, Yamamoto H. Early Clinical Outcomes of Wavefront-Guided Myopic LASIK Treatments Using a New-Generation Hartmann-Shack Aberrometer. Journal of Refractive Surgery. 2014 Jan; 30(1):14-21.
2. Schallhorn S, Venter J, Hannan S, Hettinger A. Outcomes of wavefront guided LASIK using a new-generation Hartmann-Shack aberrometer in patients with high myopia. Journal of Cataract and Refractive Surgery. In Press.