SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Intraocular Telescope
Device Trade Name:	Implantable Miniature Telescope IMT(by Dr. Isaac Lipshitz)
Applicant's Name and Address:	VisionCare Ophthalmic Technologies, Inc. 14395 Saratoga Ave., Suite 150 Saratoga, CA 95070 (408) 872-9393 (phone) (408) 872-9395 (fax)
Date of Panel Recommendation:	March 27, 2009
PMA Number:	P050034
Date of Good Manufacturing Practice Inspection:	May 6, 2010
Date of Notice of Approval to Applicant:	July 1, 2010
Expedited:	FDA granted expedited review status October 17, 2005 for the following reason: the IMT will treat an irreversibly debilitating condition where approved alternatives exist, but where the IMT provides for potentially significant advances in effectiveness over existing alternatives.

II. INDICATIONS FOR USE

VisionCare's Implantable Miniature Telescope (by Dr. Isaac Lipshitz) (intraocular telescope) is indicated for monocular implantation to improve vision in patients greater than or equal to 75 years of age with stable, severe to profound vision impairment (best corrected distance visual acuity 20/160 to 20/800) caused by bilateral central scotomas associated with end-stage age-related macular degeneration (AMD).

Patients must:

- have retinal findings of geographic atrophy or disciform scar with foveal involvement, as determined by fluorescein angiography.
- evidence of visually significant cataract (≥ Grade 2).
- agree to undergo pre-surgery training and assessment (typically 2 to 4 sessions) with low vision specialists (optometrist or occupational therapist) in the use of an external telescope sufficient for patient assessment and for the patient to make an informed decision.
- achieve at least a 5-letter improvement on the ETDRS chart with an external telescope.

- have adequate peripheral vision in the eye not scheduled for surgery.
- agree to participate in postoperative visual training with a low vision specialist.

RESTRICTIONS

RESTRICTED DEVICE: U.S. Federal Law restricts this device to sale, distribution, and use by or on the order of a physician or other licensed practitioner.

Before first implanting the intraocular telescope, physicians must participate in the required portion of the Physician Training Program provided by VisionCare.

III. CONTRAINDICATIONS

Implantation of the intraocular telescope is contraindicated in patients:

- with Stargardt's macular dystrophy.
- with central anterior chamber depth (ACD) <3.0 mm; measurement of the ACD should be taken from the posterior surface of the cornea (endothelium) to the anterior surface of the crystalline lens.
- with the presence of corneal guttata.
- who do not meet the minimum age and endothelial cell density (ECD) requirements, as shown in the grid in Table 1:

TABLE 1
BASELINE ENDOTHELIAL CELL DENSITY

Age Range	75-84	85 or Greater
Minimum Cell Density	2000	1800

The minimum baseline endothelial cell counts described in Table 1 are based on endothelial cell loss assumptions calculated from the upper 90% confidence limits observed in the PMA clinical trial, in guttata-free eyes with anterior chamber depth ≥ 3.0 mm. Additional considerations were average life expectancies based and end-of-life ECD of 750 cells/mm^2 to maintain corneal clarity, although the exact ECD needed is not known and varies from patient to patient. Patients with endothelial cell counts lower than the minimum cell density shown in the grid may have a higher risk of developing low ECD levels and corneal edema before end of life. Even patients who have baseline ECD above the levels shown in Table 1 may be at risk of corneal transplant if ECD loss due to surgery is high, the chronic rate of ECD loss is high, or if life span is longer than average.

The device is also contraindicated in patients:

- with cognitive impairment that would interfere with the ability to understand and complete the Acceptance of Risk and Informed Decision Agreement or prevent proper visual training/rehabilitation with the device.
- who have evidence of active choroidal neovascularization (CNV) on fluorescein angiography or treatment for CNV within the past six months.

- with any ophthalmic pathology that compromises the patient's peripheral vision in the fellow eye.
- with previous intraocular or cornea surgery of any kind in the operative eye, including any type of surgery for either refractive or therapeutic purposes.
- who have prior or expected ophthalmic related surgery within 30 days preceding intraocular telescope implantation.
- with a history of steroid-responsive rise in intraocular pressure (IOP), uncontrolled glaucoma, or preoperative IOP >22 mm Hg, while on maximum medication.
- with known sensitivity to post-operative medications.
- who have a history of eye rubbing or an ocular condition that predisposes them to eye rubbing.
- in whom the planned operative eye has:
  - Myopia > 6.0 D
  - Hyperopia > 4.0 D
  - Axial length < 21 mm
  - A narrow angle, i.e., < Schaffer grade 2
  - Cornea stromal or endothelial dystrophies, including guttata
  - Inflammatory ocular disease
  - Zonular weakness/instability of crystalline lens, or pseudoexfoliation
  - Diabetic retinopathy
  - Untreated retinal tears
  - Retinal vascular disease
  - Optic nerve disease
  - A history of retinal detachment
  - Intraocular tumor
  - Retinitis pigmentosa.

- In eyes in which both haptics cannot be placed within the capsular bag during surgery, the intraocular telescope should be removed and replaced with a conventional intraocular lens (IOL); sulcus fixation of either one or both haptics increases the risk of severe endothelial cell loss and corneal transplant.

IV. WARNINGS AND PRECAUTIONS

- Patients undergoing intraocular telescope implant may be at risk of developing persistent unresolved corneal edema (edema that continues), persistent vision-impairing corneal edema (continuing corneal edema leading to a loss of best corrected distance visual acuity (BCDVA) > 2-lines from baseline level at last available visit) and may need corneal transplantation. In up to 5 years of follow-up there were:
  - 10 reports of persistent unresolved corneal edema (cumulative probability 9.2%, 95% confidence interval 3.3%, 15.1%).
  - 8 reports of persistent vision-impairing corneal edema (cumulative probability 6.8%, 95% confidence interval 2.1%, 11.6%). Persistent

vision-impairing corneal edema is a subset of persistent unresolved corneal edema.

- 5 reports of corneal transplant (cumulative probability 4.1%, 95% confidence interval 0.4%, 7.7%). Corneal transplant is a subset of persistent unresolved corneal edema.

- Only cornea specialists should implant the intraocular telescope. A cornea specialist is an ophthalmologist who had fellowship or other specialty training in diseases and surgery of the cornea and who regularly performs cornea surgical procedures such as penetrating keratoplasty.
- The potential for the device to alter IOP and long-term risk of glaucoma, anterior synechiae, and pigment dispersion are unknown.
- Surgical difficulties at the time of cataract extraction might increase the potential for complications, including persistent bleeding, significant iris damage, uncontrolled positive pressure, or significant vitreous prolapse or loss.
- Secondary surgical intervention may be necessary and include intraocular telescope repositioning, removal, corneal transplant, or intraocular telescope replacement.
- A small percentage of patients (< 4% in the clinical trial) may be dissatisfied to the point that they request and have the device explanted.
- Thermal lasers should be used with extreme caution around the device and never through the glass optical portion. Accidental focus of the laser beam on any glass part could cause glass fracture.
- Patients must be informed that participation in visual training is necessary to maximize the benefit of the change in visual status.
- The intraocular telescope protrudes slightly through and above the plane of the iris. Patients must be informed that eye rubbing must be avoided due to risk of endothelial cell loss. Patients who are persistent eye rubbers are contraindicated.
- The intraocular telescope restricts the patient's peripheral field. The functional field of view will be generally limited to that of the non-implanted eye.
- The intraocular telescope implant is MR-Conditional (see "Note" in Section VII for conditions).

Providing Information to the Patient and Obtaining the Patient's Agreement

- Before a patient decides whether to have implantation of the intraocular telescope, he or she should be given a copy of the Patient Information Booklet and advised to read it or have it read to him or her by a family member or friend. The patient should be given sufficient time to consider whether he or she wishes to have the procedure. The patient should be given ample opportunity to ask questions and get answers from his/her referring ophthalmologist, the surgeon, eye care professionals at their offices, and family and friends.
- A physician or other health care professional should assess whether the patient is able to consider the benefits and risks of intraocular telescope implant. The patient should be implanted with the intraocular telescope only after the patient,

with full opportunity for consideration of the Patient Information Booklet, has signed the Acceptance of Risk and Informed Decision Agreement.

- Since the effectiveness of the preoperative screening and postoperative training programs used in the clinical trial were not systematically investigated in the clinical trial, their ability to predict candidates who will benefit from intraocular telescope implantation is unknown.

Precautions Concerning the Risks of Implantation of the Intraocular Telescope

- The effects of the intraocular telescope on the corneal endothelium beyond five years have not been established. Patients should undergo an eye exam at least once a year. This examination should include specular microscopy, to determine whether the cornea is at risk of edema. Physicians should use clinical judgment regarding any interventions related to endothelial cell density changes. The clinical study results for outcomes associated with explantation of the intraocular telescope should be reviewed.
- Intraocular telescope dimensions necessitate a 12 mm limbal incision and 7 mm capsulorhexis for implantation. Special care should be taken to minimize the risk of endothelial cell loss including attention to proper patient selection and appropriate surgical techniques.
- As with any surgical procedure, risk is involved. Potential complications accompanying crystalline lens removal and intraocular telescope implantation surgery may include, but are not limited to: cornea endothelial cell loss leading to corneal edema, corneal transplant, choroidal detachment, choroidal hemorrhage, microbial infection, retinal detachment, vitreous loss, posterior capsular rupture, intraocular inflammation, uveitis, etc.
- Inaccurate or unreliable measures of corneal endothelial cell density should be avoided. A non-contact specular microscope should be used for determining central corneal endothelial cell density. The images should provide distinct countable cells and contain a minimum of 100 identifiable cells. Three images of the central cornea should be taken and the results averaged. Specific instructions by the microscope manufacturer for taking images and endothelial cell density calculation should be followed.
- Patients with corneal endothelial cell coefficient of variation >0.45 may have a stressed endothelial cell layer, and may be prone to greater than normal endothelial cell loss if implanted with the intraocular telescope.
- Patients with corneal endothelial cell percent hexagonality <45% may have stressed endothelial cell layer, and may be prone to greater than normal endothelial cell loss if implanted with the intraocular telescope.
- Vision-related quality of life may not improve. 48.2% of patients did not report a clinically significant improvement in the National Eye Institute (NEI) Visual Function Questionnaire (VFQ) composite score. 22.3% of patients (43/193) lost at least 5 points in VFQ-25 composite score from baseline and 25.9% (50/193) of patients reported no significant change (i.e., change within ± 5 points).

Surgical techniques and other factors that may lead to increased ocular complications or corneal endothelial cell loss include, but are not limited to:

- Forcing the intraocular telescope into the anterior chamber through an incision that is too small.
- Corneal endothelial touch with surgical instruments, the intraocular telescope, or other intraocular matter.
- Excessive stretching (e.g., 'tenting') of the cornea.
- Inadequate intra-operative anterior chamber space management or peri-operative wound management leading to shallow chamber.
- Placing one or both carrier haptics outside of capsular bag (i.e., sulcus); this may result in a tilted device and greater risk of endothelial cell loss.
- Inadequate use of ocular viscoelastic devices.

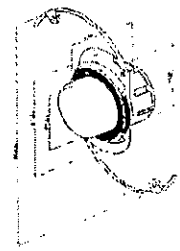
Monocular intraocular telescope implantation will result in the following visual effects:

- The size difference in the retinal images in the central field will be too great to fuse binocularly.
- Non-corresponding images in the two eyes will produce either double vision or binocular rivalry and suppression effects whenever both eyes are open.
- The differences in image size, motion, and brightness in the two eyes may promote diplopia by disrupting the normal neural mechanisms and feedback circuits that control binocular eye position and movements. Diplopia was reported in 4 (1.8%) of the subjects implanted with the intraocular telescope. Some subjects may find it difficult to judge the true position of objects in the environment under these conditions.
- Implantation of the intraocular telescope will limit the field of view in the implanted eye to 24° (WA 2.2X) or to 20° (WA 2.7X).
- The binocular temporal field will be obstructed on the side of the intraocular telescope-implanted eye, and the limits of the binocular field are the same as those of the monocular field of the fellow eye.
- When the intraocular telescope field suppresses the overlapping region of the fellow eye field, vision will be obstructed in the annular region of the binocular visual field between the unmagnified and magnified outer limit of the intraocular telescope field, i.e., between eccentricities of 12° and 26.4° for the WA 2.2X model and 10° and 27° for the WA 2.7X model.
- Beyond the image projected onto the retina, approximately 55°, the implanted eye will experience a permanent loss of patterned input to the peripheral retina. The implications of this are unknown.
- The magnified retinal image in the intraocular telescope implanted eye will move faster than the retinal image in the fellow eye during consensual eye movements. The impact of this motion discrepancy is unknown. While nystagmus, disorientation and loss of balance were not reported by subjects implanted with the intraocular telescope in the clinical trial, the impact of the intraocular telescope implantation on the vestibular system was not evaluated.

- Retinal illuminance in the intraocular telescope implanted eye will be reduced by the transmission times the inverse square of the power. For the 2.2 power and 2.7 power telescopes, the respective attenuation factors are about 0.8 and 1.0 log units, comparable to wearing a monocular sunglass. Although the impact of this attenuation on visual performance was not evaluated in the clinical trial, it can be expected to reduce both contrast sensitivity and acuity in dim light conditions in the intraocular telescope implanted eye.

V. DEVICE DESCRIPTION

VisionCare's Implantable Miniature Telescope (by Dr. Isaac Lipshitz) (IMT or intraocular telescope) is an implantable device which, when combined with the optics of the cornea, constitutes a telephoto system for improvement of visual acuity in patients with severe to profound vision impairment due to bilateral, end-stage, age-related macular degeneration(AMD). The intraocular telescope is surgically implanted in the capsular bag and is held in position by haptic loops. The intraocular telescope is available in two models: Wide Angle (WA) 2.2X and Wide Angle (WA) 2.7X. Both models are indicated for monocular implant. The implanted eye provides central vision, while the fellow eye continues to be used for peripheral vision.



The intraocular telescope is composed of three primary components: a fused silica capsule that contains optical elements, a clear polymethylmethacrylate (PMMA) carrier, and a blue PMMA light restrictor. All materials are biocompatible for long-term ocular implantation per ISO 10993. One of the internal components (not in contact with body fluids or tissue) of the intraocular telescope contains stainless steel, has been evaluated for Magnetic Resonance Imaging (MRI) compatibility and determined to be MR-Conditional. Product specifications are described in Table 2.

Note: MRI testing was performed to evaluate the magnetic field interactions, heating, and artifacts of the intraocular telescope induced by a commercial 3-Tesla MRI system. Based on the MRI testing information, the intraocular telescope will not present any additional hazard or risk to a patient undergoing an MRI procedure using a scanner operating with a static magnetic field of 3-Tesla or less and under the MRI-related heating conditions used for the evaluation (MRI for 15 minutes at an MR system reported whole body averaged specific absorption rate (SAR) value of 3 W/Kg). The MRI image quality may be compromised if the area of interest is the same as or close to the position of the device (in this case, it may be necessary to optimize MR imaging parameters to compensate for the presence of the implant).

TABLE 2
PRODUCT SPECIFICATIONS

FEATURE	MODEL WA 2.2X	MODEL WA 2.7X
MAGNIFICATION	2.2x ± 10%	2.7x ± 10%
DEPTH OF FIELD	1.5 to 10 m	1.5 to 10 m
OPTIMAL FOCUSING DISTANCE	3 m	3 m
FIELD OF VIEW	Full field: 24° (Nominal), 52.8° on the retina	Full field: 20° (Nominal), 54° on the retina
DIMENSIONS		
Overall Diameter	13.5 mm	13.5 mm
Clear Aperture	3.2 mm	3.2 mm
Intraocular Telescope Diameter	3.6 mm	3.6 mm
Axial Length	4.4 mm	4.4 mm
Haptic Angulation	12.7°	12.7°
WEIGHT		
Air	115 mg + 10%	115 mg + 10%
Aqueous	60 mg + 10%	60 mg + 10%

VI. ALTERNATIVE PRACTICES OR PROCEDURES

Alternative, corrective interventions currently available are vision aids such as special spectacles and head-mounted or hand-held telescopes, which magnify images onto the retina.

VII. MARKETING HISTORY

The intraocular telescope device has not been marketed within the United States. The device has received marketing approval in the European Union. The device has not been withdrawn from marketing for any reason relating to the safety or effectiveness of the device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Data for evaluation of the intraocular telescope were provided by prospective, multi-center clinical trials; protocol IMT-002, a pivotal study and protocol IMT-002-LTM, a long-term safety study in which patients implanted under protocol IMT-002 were followed through 5 years. The objective of the 2-year, prospective, 28-center IMT-002 study (n=217) was to evaluate the safety and effectiveness of the intraocular telescope for the improvement of visual acuity and vision-related quality of life in patients with bilateral moderate to profound central vision impairment (BCDVA between 20/80 and 20/800) due to untreatable, end-stage age-related macular degeneration.

Rates of significant adverse events reported in clinical studies IMT-002 and IMT-002-LTM are shown in Table 3.

TABLE 3
SIGNIFICANT OCULAR ADVERSE EVENTS
OPERATED EYES (N=217), STUDIES IMT-002 AND IMT-002-LTM

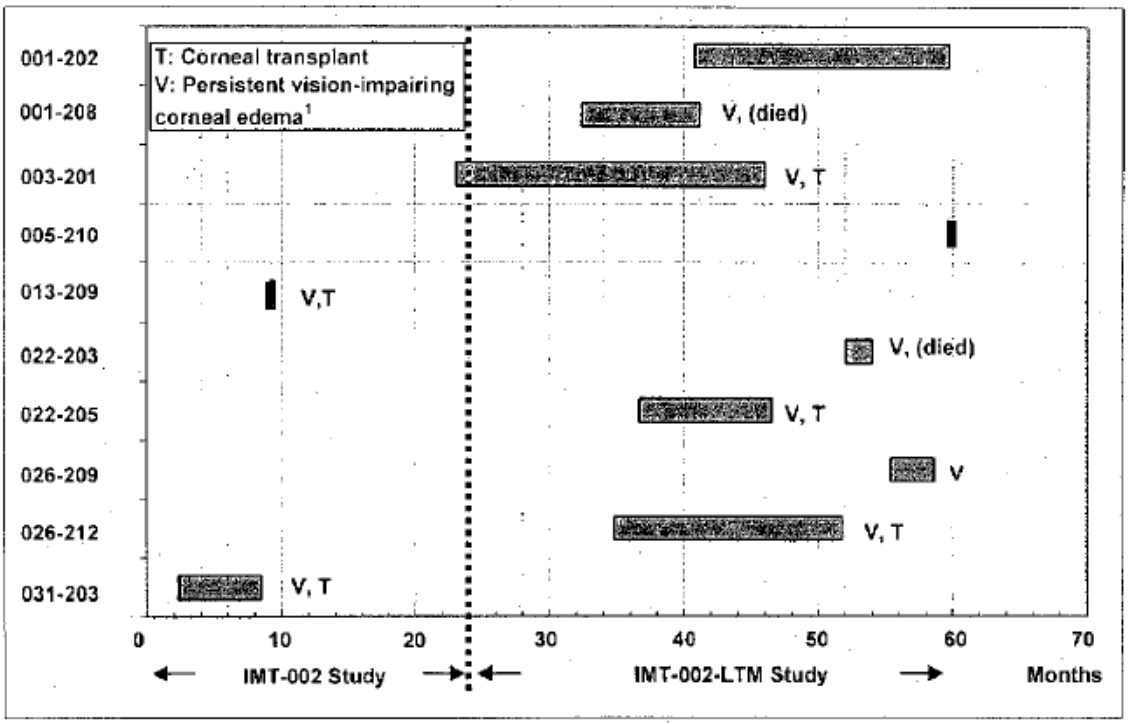
Significant Adverse Event – Device Related or Potentially Device Related	n	% (n/217)
Corneal transplant (subset of persistent[1] vision-impairing corneal edema)	5	2.3%
Persistent[1] vision-impairing[2] corneal edema (subset of persistent unresolved corneal edema)	8	3.6%
Device failure	2	0.9%
Intraocular telescope removal	12	5.5%
Decrease in BCDVA[3]	15	6.9%
Persistent[1] unresolved corneal edema (subset of corneal edema reported > 30 days after surgery)	10	4.6%
Corneal edema reported > 30 days after surgery*	14	6.5%
Intraocular telescope dislocation	4	1.8%
Significant Adverse Event – Other		
Choroidal neovascularization	5	2.3%
Endophthalmitis	0	0%
Retinal detachment	0	0%
Retinal tear	0	0%

[1] Persistent – continuing
[2] Vision-impairing – decrease in BCDVA > 2 lines from baseline at the last available visit
[3] Decrease in BCDVA - decrease in BCDVA > 2 lines from baseline at the last available visit
*Corneal edema reported in 13 intraocular telescope-implanted eyes and in 1 operated eye not implanted with an intraocular telescope

Information on less serious adverse events and on complications associated with the intraocular telescope is provided in Section XII (Clinical Study Results) of this SSED.

The timing of observation of persistent unresolved corneal edema for the 10 intraocular telescope-implanted eyes is shown in Figure 1. Of these 10 eyes, 8 developed persistent vision-impairing corneal edema. When ECD levels fall too low (< 750 mm^2), the cornea may become edematous, thicken and lose transparency, and corneal transplantation may be needed. Five intraocular telescope implanted eyes underwent corneal transplantation. The endothelial cell density needed to maintain corneal transparency is unknown and varies from patient to patient.

FIGURE 1
INTRAOCULAR TELESCOPE-IMPLANTED EYES WITH PERSISTENT UNRESOLVED EDEMA
TIME OF OBSERVATION OF CORNEAL EDEMA



[1]Persistent vision-impairing corneal edema (continuing corneal edema leading to a loss of BCDVA > 2-lines from baseline level at last available visit)

As shown in Figure 1, most cases (8 of 10) of edema first appeared later postoperatively (at >18 months postoperatively), rather than in the early postsurgical time period.

RISK OF MAJOR EVENTS RELATED TO ENDOTHELIAL CELL LOSS, CORNEAL EDEMA, AND VISION LOSS

Using Kaplan-Meier survival analysis, the risk to an individual patient of some of the more serious adverse events was estimated for a 5-year postoperative period. (This analysis takes into account the loss to follow-up during the study.) As shown in Table 4, the cumulative probability of persistent unresolved corneal edema over 5 years was 9.2%. For persistent vision-impairing corneal edema, a subset of persistent unresolved corneal edema, the cumulative probability for this adverse event of 6.8%. Persistent vision-impairing corneal edema may require corneal transplant. There were 8 cases of persistent vision-impairing corneal edema in the study; 2 of these patients died without corneal transplant and 1 patient did not receive a transplant (reason unknown). There were 5 observed cases of corneal transplant in the study. The cumulative probability of corneal transplant over 5 years was 4.1%.

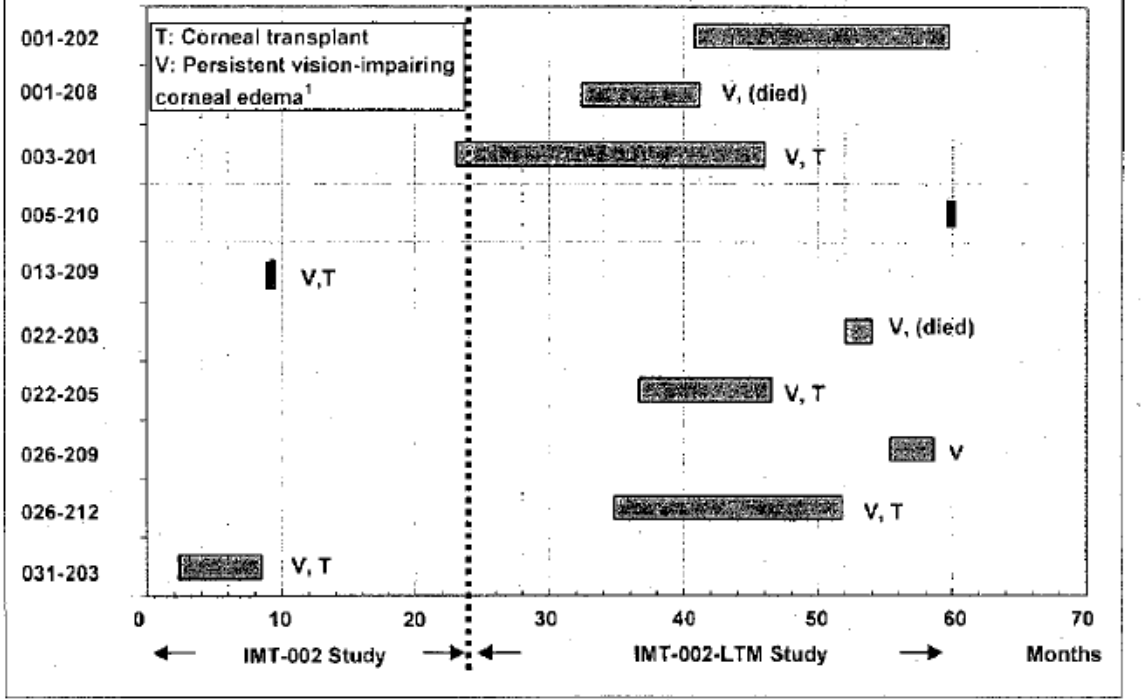

T: Corneal transplant
V: Persistent vision-impairing corneal edema[1]
001-202
001-208
003-201
005-210
013-209
022-203
022-205
026-209
026-212
031-203
V, (died)
V, T
V,T
V, (died)
V, T
V
V, T
V, T
0
10
20
30
40
50
60
70
IMT-002 Study
IMT-002-LTM Study
Months

TABLE 4
CUMULATIVE NUMBER OF EVENTS AND PROBABILITY OF PERSISTENT UNRESOLVED CORNEAL EDEMA AND THE SUBSETS OF PERSISTENT VISION-IMPAIRING CORNEAL EDEMA AND CORNEAL TRANSPLANT
206 INTRAOCULAR TELESCOPE-IMPLANTED EYES
STUDIES IMT-002 AND IMT-002-LTM

Years from Implant	Persistent Unresolved Corneal Edema		Persistent Vision-Impairing Corneal Edema[1]		Corneal Transplant[2]	
	Cum # of Events	Cum Prob[3]	Cum # of Events	Cum Prob[3]	Cum # of Events	Cum Prob[3]
	95% CI of Cum Prob		95% CI of Cum Prob		95% CI of Cum Prob	
1.0 Year (365 Days)	2	1.0%	2	1.0%	2	1.0%
	(0.0%, 2.4%)		(0.0%, 2.4%)		(0.0%, 2.4%)	
2.0 Years (730 Days)	3	1.8%	2	1.0%	2	1.0%
	(0.0%, 3.8%)		(0.0%, 2.4%)		(0.0%, 2.4%)	
3.0 Years (1095 Days)	5	3.4%	3	1.8%	2	1.0%
	(0.4%, 6.4%)		(0.0%, 3.9%)		(0.0%, 2.4%)	
4.0 Years (1461 Days)	7	5.1%	6	4.6%	4	2.9%
	(1.3%, 8.8%)		(0.9%, 8.3%)		(0.0%, 5.9%)	
5.0 Years (1914 Days)	10	**9.2%**	8	**6.8%**	5	**4.1%**
	(3.3%, 15.1%)		(2.1%, 11.6%)		(0.4%, 7.7%)	

1 Persistent vision-impairing corneal edema with BCDVA loss > 2 lines from baseline at the last available visit. This is a subset of persistent unresolved corneal edema.
2 This is a subset of persistent unresolved corneal edema
3 Cum Prob = cumulative Kaplan-Meier probability that a patient experienced the event. For each reported event, the onset date (or the first reported date) was used for patient reported events. For patient without the events, the last available dates during the study were used and treated as censored records.
4 3 of the 8 patients with vision-impairing unresolved corneal edema did not have corneal transplants; (2 patients died before undergoing transplant and corneal transplantation was not performed in the third patient)

As shown in Table 5, the cumulative probability of persistent ECD <1000 cells/mm^2 or <750 cells/mm^2 at 5 years post intraocular telescope was 20.2% and 11.8% respectively. The cumulative probability of a patient experiencing a loss of greater than 2 lines of best corrected distance visual acuity over five years was 12.3%.

TABLE 5
CUMULATIVE NUMBER OF EVENTS AND PROBABILITY OF PERSISTENT ECD < 1000 CELLS/MM[1] OR < 750 CELLS/MM[2] BCDVA LOSS > 2 LINES AT LAST VISIT 206 INTRAOCULAR TELESCOPE-IMPLANTED EYES STUDIES IMT-002 AND IMT-002-LTM

Years from Implant	Persistent ECD < 1000[1] cells/mm^2		Persistent ECD < 750[2] cells/mm^2		BCDVA Loss > 2 Lines[3] at Last Visit	
	Cum # of Events	Cum Prob[4]	Cum # of Events	Cum Prob[4]	Cum # of Events	Cum Prob[4]
	95% CI of Cum Prob		95% CI of Cum Prob		95% CI of Cum Prob	
1.0 Year (365 Days)	23	11.5%	13	6.5%	4	2.0%
	(7.1%, 15.9%)		(3.1%, 9.9%)		(0.1%, 3.9%)	
2.0 Years (730 Days)	27	13.8%	17	8.6%	5	2.6%
	(9.0%, 18.7%)		(4.7%, 12.6%)		(0.3%, 4.8%)	
3.0 Years (1095 Days)	27	13.8%	17	8.6%	6	3.4%
	(9.0%, 18.7%)		(4.7%, 12.6%)		(0.7%, 6.1%)	
4.0 Years (1461 Days)	33	19.1%	18	9.5%	11	7.8%
	(13.0%, 25.2%)		(5.3%, 13.8%)		(3.2%, 12.4%)	
5.0 Years (1914 Days)	34	**20.2%**	20	**11.8%**	15	**12.3%**
	(13.8%, 26.6%)		(6.6%, 16.9%)		(6.2%, 18.5%)	

1 ECD < 1000 at two consecutive visits or at the last available visit.

2 ECD < 750 at two consecutive visits or at the last available visit.

3 BCDVA loss > 2 lines from baseline at the last available visit.

4 Cum Prob = cumulative Kaplan-Meier probability that a patient experienced the event. For each reported event, the onset date (or the first reported date) was used for patient reported events. For patient without the events, the last available dates during the study were used and treated as censored records.

Note that the risk for new events increased over time during the first 5 years and may continue to increase.

IX. SUMMARY OF PRECLINICAL STUDIES

Preclinical studies performed on the intraocular telescope were consistent with the FDA draft guidance document for refractive implants dated August 1, 2000. VisionCare conducted a battery of *in vivo* and *in vitro* acute and chronic toxicity tests that established

the biocompatibility of intraocular telescope materials. These studies, combined with data from chemistry and engineering analyses, demonstrate the suitability of the materials and overall device design for use as an intraocular implant. The adequacy of the manufacturing processes, including sterilization, was established through review of the manufacturing information in the PMA as well as through on-site inspection. Preclinical testing demonstrates safety and effectiveness of the intraocular telescope from the microbiology, toxicology, engineering, and manufacturing perspectives.

Biocompatibility – Biological testing

A summary of the biocompatibility testing that the sponsor performed to support the safe use of the IMT is provided in the table below. The sponsor has conducted all testing in conformance with the relevant sections of International Organization for Standardization (ISO) 10993 and ISO 11979. Additionally, the sponsor has conducted all testing in conformance with Good Laboratory Practices (GLP) regulations. Testing was performed on ethylene oxide (EO) sterilized finished IMTs or a "mock device" that is a replica of the original product. The device passed all biocompatibility tests in the table below.

Test	Method	Extract(s)
Cytotoxicity	ISO Agarose Overlay	"Solid"
		Saline
		YAG Laser extract (saline)
	Inhibition of Cell Growth (1 point)	Water for Injection
	MEM Elution	Minimum Essential Medium
Systemic	USP and ISO Systemic Toxicity	Saline, sesame oil
Implantation	ISO Muscle Implantation Study (30 days and 12 weeks)	N/A
	Rabbit Ocular Implantation (6 months)	N/A
Genotoxicity	Ames Test	Ethanol, saline
	In Vitro Chromosomal Aberration Study	McCoy's 5A Medium
	Mouse Bone Marrow Micronucleus Study	Saline, sesame oil
Irritation, Sensitization	ISO Ocular Irritation	Saline
	Murine Local Lymph Node Assay	Saline, DMSO

Note: The cytotoxicity test on the YAG laser extract and the six month animal implantation tests were conducted on finished devices rather than "mock IMTs."

An in vivo intraocular implantation study was conducted in rabbits for a six month period. The control device was a PMA approved PMMA IOL. The test and control lenses were surgically implanted in the posterior chamber of 10 rabbits following phacoemulsification of the natural lens (test lens in one eye, PMMA lens in contralateral eye). The eyes were evaluated by slit lamp examination according to a modified McDonald-Shadduck scoring system, and slit lamp exams were conducted preoperatively, on days 1, 3, 7, weeks 2 through 4, and biweekly until 6 months postop.

At 6 months postop, the rabbits were euthanized and the eyes were enucleated and submitted for histopathological examination.

Macroscopic examinations revealed no ocular irritation trends that would be considered clinically significant effects from the test article. Microscopic evaluations of the ocular tissue sections revealed no adverse effects directly related to the test article. The changes in the lens capsules and the presence of regenerative and degenerative lenticular fibers were present for both test and control eyes and are related to the animal model used rather than a treatment effect. There were no significant differences between the eyes that received the test versus the control article.

Biocompatibility - Physico-chemical testing

The sponsor performed the following physico-chemical testing as described in the ISO biocompatibility standard 11979-5.

i. Extractables – The extraction was performed in purified water and then in chloroform at 37 degrees C for 72 hours. The sponsor has summarized the results as follows: High Performance Liquid Chromatography (HPLC) analysis showed no hydroxyethylmethacrylate (HEMA) detected in the purified water blank or test extract solutions (the chloroform blank and test extract solutions were analyzed but had peaks that interfered with the detection of HEMA and other compounds); GC/MS (Gas Chromatography/Mass Spectrometry) analysis showed no semi-volatile organic compounds in the blank or test extract solutions; Inductively Coupled Plasma (ICP) analysis showed that the metals/elements analyzed were all below the detectable level with the exception of Boron and Silicon (the concentrations were 1.86 ppm and 1.41 ppm, respectively); Ultraviolet (UV) spectroscopy identified no extractable substances in the purified water extract, gravimetric determination showed that the change in mass following the purified water and chloroform extractions was 0.00016g and 0.22353g, respectively. This study is acceptable and demonstrates that the levels of extractables are very low.

ii. Hydrolytic stability – This study looks for the degradation products due to hydrolysis. The testing was performed at 37° C and 50 ° C for 30 and 90 days. The sponsor has summarized the results as follows: HPLC analysis showed no HEMA detected; GC/MS analysis showed no semi-volatile organic compounds; ICP analysis showed that the metals/elements analyzed were all below the detectable level; UV spectroscopy identified no extractable substances, gravimetric determination showed that the change in mass following each extraction was <0.00041 g. This study is acceptable and demonstrates that this device is hydrolytically stable.

iii. Exhaustive extraction – This testing was performed using hexane to determine the total amount of extractable material from the device. The sponsor has summarized the results as follows: The analysis of the hexane extracts showed the percentage

of material extracted from the test material was 0.02%. This test is acceptable and demonstrates that the total extractables in the device are very low.

iv. Photostability –The sponsor has performed the photostability testing in conformance with the procedures described in ISO 11979-5. No evidence of instability in the absorbance properties or release of toxic compounds was observed.

v. Nd:YAG testing – The devices were placed in vials with 2 ml of saline and were subjected to laser damage at a power of 5.1 mJ for 50 hits on the periphery of the test article. The sponsor noted that the laser beam did not pass through the glass portion of the test article. The sponsor has summarized the results as follows: HPLC analysis showed no HEMA detected; GC/MS analysis showed no semi-volatile organic compounds; ICP analysis showed that the metals/elements analyzed were all below the detectable level with the exception of Boron and Silicon (the concentrations were 4.4 ppm and 5.4 ppm, respectively); and UV spectroscopy identified no extractable substances. The study demonstrates that the Nd:YAG does not damage the periphery of the IMT. The sponsor is recommending that the laser not be focused through the central portion of the IMT as this would cause damage to the device. Therefore, no evaluation was performed to determine if the laser could be focused through the optical portion of the IMT.

Sterilization, Packaging and Shelf Life

The IMT is packaged in a protective case with cap, and then placed into a blister pack with a Tyvek lid, and ethylene oxide sterilized for a sterility assurance level calculated to 10^{-6}. FDA has no remaining concerns regarding the sterilization of the IMT – all issues were resolved in PMA P050034.

The sponsor has proposed a 24 month shelf life for the IMT. FDA has no remaining issues regarding the shelf life at 24 months - all issues were resolved in PMA P050034.

X. SUMMARY OF CLINICAL STUDIES

Data for evaluation of the intraocular telescope were provided by prospective, multi-center clinical trials, protocol IMT-001, a safety and preliminary effectiveness feasibility study, protocol IMT-002, a pivotal study and protocol IMT-002-LTM, a long-term safety study in which patients implanted under protocol IMT-002 were followed through 5 years. The objective of the 2-year, prospective, 28-center IMT-002 study (n=217) was to evaluate the safety and effectiveness of the intraocular telescope for the improvement of visual acuity and vision-related quality of life in patients with bilateral moderate to profound central vision impairment (BCDVA between 20/80 and 20/800) due to untreatable, end-stage age-related macular degeneration.

TABLE 6
INTRAOCULAR TELESCOPE CLINICAL STUDIES

Clinical Study	Study Design	Objective	Number of Sites	Number of Subjects
Protocol IMT-001 Feasibility	Prospective, single-arm, open, multi-center	Evaluate the safety and preliminary effectiveness of the intraocular telescope	3	15 enrolled 14 implanted
Protocol IMT-002 Pivotal	Prospective, single-arm, open, multi-center trial	Evaluate the safety & effectiveness of the intraocular telescope	28	217 enrolled 206 implanted
Protocol IMT-002-LTM Long-Term Monitoring	Prospective single-arm, open, multicenter trial	Conduct long-term safety monitoring of a cohort of patients enrolled in IMT-002	25	129 enrolled

A. Pivotal Clinical Study Design

The clinical study that formed the basis for FDA's finding that the intraocular telescope is safe and effective for its intended use was a prospective, multi-center, single-arm, open (unmasked) clinical trial designed to evaluate the safety and effectiveness of the intraocular telescope for the improvement of visual acuity in patients with bilateral moderate to profound central vision impairment (BCDVA between 20/80 and 20/800) due to untreatable, end-stage age-related macular degeneration.

A cohort of patients from the IMT-002 study population were enrolled in the IMT-002-LTM (n=129) study to collect and report long-term safety of the intraocular telescope through 5 years.

STATISTICAL ANALYSIS PLAN

The sample size for effectiveness for this study was calculated based on the following considerations.

• The statistical hypotheses for the primary effectiveness endpoint was:
H0: the proportion of eyes with an improvement of 2 lines or more in either distance or near BCVA at 12 months

Postoperatively (Pt) $\leq$ 0.5 (50%) versus Ha: Pt > 0.5.

Assuming -

- that Pt equals 60%,
- A level of significance (alpha) of 0.05,

- A statistical power of 80%, and
- A dropout rate of 20%,

- the sample size for the primary effectiveness endpoint was calculated to be 198 implanted eyes.

The sample size for safety was calculated based on the following considerations:

- A review of the published literature found that a mean endothelial cell loss of 10-17% within one year after surgery was observed for large incision surgeries.
- The statistical hypotheses for the primary safety endpoint was:

  H_0: the mean percent endothelial cell loss at 12 months postop (μ) > 17% versus Ha: μ < 17%.

Assuming:

- The standard deviation of percentage loss is17.5%.
- A level of significance (α) of 0.05,
- The statistical power is 80%,
- the expected mean loss of 13.5%)
- A normal distribution of cell losses, and
- a dropout rate of 20%,

the sample size for the primary safety endpoint was calculated to be 195 eyes.

Therefore, the necessary number of implanted eyes was 198 eyes to fulfill both requirements. With this sample size, there is a 95% confidence level to observe at least one adverse event at a rate of 1.5%.

STUDY PROCEDURES

Consented subjects underwent a baseline evaluation to determine eligibility for the study. A component of the baseline evaluation consisted of evaluation with 2.2X and 3.0X external telescopes. Both telescopes were used by the study site to evaluate subjects' vision improvement with the external telescope. A 2.2X external telescope was given to potential subjects to utilize at home for a period of at least three days to provide a simulation of visual acuity that may be achieved with the IMT while attempting routine daily tasks.

Subjects underwent intraocular telescope implantation performed using either a limbal insertion technique or a scleral tunneling procedure. Anesthesia was induced by retrobulbar or peribulbar injection, and mydriatic agents were administered to ensure adequate pupil dilation during surgery. Limbal intraocular telescope insertion was performed through a 10 to 12 mm incision made at 120° to 160° arc length. For scleral tunnel insertion, an incision at least 10 mm in length was performed 2.5 to 3 mm

posterior to the limbus. A tunnel was then created which opened into the anterior chamber at the limbus. A paracentesis was performed, and viscoelastic was injected into the anterior chamber. A continuous curvilinear capsulorrhexis of approximately 6.5 mm was made in the lens capsule. Additional viscoelastic was injected into the anterior chamber and the capsular bag, and used to coat the intraocular telescope. The intraocular telescope was implanted by placing both loops inside the capsular bag, suturing the cornea and rotating the loops of the intraocular telescope to the 12:6 o'clock position. The viscoelastic was removed, the pupil was constricted, a peripheral iridectomy was performed and the incision was tested for leakage.

A sub-Tenon's injection of betamethasone depot (or appropriate substitute) was administered at the end of surgery. Additionally, a standardized course of topical antibiotic and nonsteroidal anti-inflammatory was administered at the end of surgery and continued per product labeling for at least 2 days. Prednisolone acetate (1%) or equivalent was to be administered every 2 waking hours for the first two weeks post-implantation, followed by administration every 4 waking hours for 2-4 weeks, tapering over the next 4 to 6 weeks for a total duration of postoperative steroid treatment of approximately 3 months. Homatropine 5% or a similar drug was to be administered twice daily for 4 to 6 weeks postoperatively. If homatropine was inadequate to maintain cycloplegia, the use of atropine was allowed.

Study investigators were directed to exercise clinical judgment in determining whether a more moderate or rapid tapering of the topical steroid regimen was indicated for some subjects, particularly in eyes with signs of medicamentosa.

EXTERNAL EVALUATION GROUPS

An independent, central reading center at Emory University Department of Ophthalmology analyzed the specular micrographs obtained from the study population for endothelial cell density. Endothelial cell morphology and morphometry were evaluated to determine the percentage of hexagonal cells and the coefficient of variation.

1. PROTOCOL INCLUSION AND EXCLUSION CRITERIA

Enrollment in the study was limited to patients who met the following key eligibility criteria:

INCLUSION CRITERIA

- Bilateral, stable, untreatable central vision disorders (untreatable AMD or Stargardt's macular dystrophy) as determined by fluorescein angiography.
- Cataract.
- BCDVA between 20/80 and 20/800, and adequate peripheral vision in one eye (the non-implanted eye) to allow navigation.
- Achievement of at least a five-letter improvement on the ETDRS chart with an external telescope in the eye scheduled for surgery.
- Anterior chamber depth of ≥ 2.5mm in the operative eye.

- Available for the study duration of approximately 24 months and willing to return for all visits for training and evaluation.
- Alert, mentally competent, and able to understand and comply with the requirements of the clinical trial, and personally motivated to abide by the requirements and restrictions of the clinical trial.
- At least 55 years of age.

EXCLUSION CRITERIA

- Evidence of active CNV on fluorescein angiography or treatment for CNV within the past six months.
- Anticipated need for cataract extraction and intraocular lens implantation during the first
  12 months following intraocular telescope implantation in the fellow eye. Any anticipated cataract extraction had to be performed at least 30 days prior to enrollment in the clinical study.
- Ophthalmic related surgery within the 30 days preceding implantation of the IMT.
- Any of the following conditions in the operative eye:
  - Myopia > 6.0 D
  - Hyperopia > 4.0 D
  - Axial length < 21 mm
  - Endothelial cell density < 1600 cells/mm^2
  - Narrow angle, i.e., less than Shaffer grade 2
  - Cornea stromal or endothelial dystrophies or disorders
  - Inflammatory ocular disease
  - Zonular weakness/instability of crystalline lens
  - Pseudoexfoliation
  - Diabetic retinopathy
  - Untreated retinal tears
  - Retinal vascular disease
  - Optic nerve disease
  - History of retinal detachment
  - Retinitis pigmentosa
  - Any intraocular tumor and medical or ophthalmic condition that in the opinion of the Investigator rendered the subject unsuitable for participation in the study.
- Any ophthalmic pathology that compromised the patient's peripheral vision in the fellow eye.
- Any ocular condition that predisposed the patient to eye rubbing.
- Significant communication impairments or severe neurological disorders that prevented or interfered with the study requirements.
- Previous intraocular or corneal surgery of any kind in the operative eye(s), including any type of surgery for either refractive or therapeutic purposes.
- History of steroid-responsive rise in intraocular pressure, uncontrolled glaucoma, or preoperative IOP >22 mm Hg.
- Known sensitivity to planned study concomitant medications.

- Participation in any other ophthalmic drug or device clinical trial during the time of this clinical investigation.

2. Follow-up Schedule

Postoperatively, study subjects were examined and evaluated according to the following schedule of visits:

Day 1	24 to 36 hours postoperative
Day 7	4 to 10 days postoperative
1 month	2 to 6 weeks postoperative
3 months	6 to 18 weeks postoperative
6 months	18 to 32 weeks postoperative
9 months	32 to 44 weeks postoperative
12 months	44 to 56 weeks postoperative
18 months	66 to 78 weeks postoperative
24 months	90 to 102 weeks postoperative

Study subjects were scheduled for vision training at Weeks 1, 2, 4, 6, 10 and 12.

The clinical parameters evaluated at study examinations were:

- Slit lamp examination
- Best spectacle-corrected distance visual acuity
- Best spectacle-corrected near visual acuity
- Intraocular pressure
- Central corneal thickness
- Specular microscopy
- Complications, adverse events and device malfunctions.
- VFQ-25 questionnaire & Activities of Daily Life (ADL).

Postoperative visual examinations were performed by the investigator or a designee such as ophthalmic technicians, optometrists, and/or ophthalmologists under the supervision of the investigator using methods described in the study protocol. All preoperative and postoperative examinations were performed using similar pieces of equipment at each site.

3. Clinical Endpoints

With regards to safety, percentage loss in the endothelial cell counts was to be calculated for each eye. The Student t test was to be used for testing the mean percentage cell loss. The main analysis intended to demonstrate that the mean percentage loss was less than 17%.

With regards to effectiveness, the primary endpoint was the proportion of eyes with at least a 2-line improvement in either distance or near Best Spectacle Corrected Visual

Acuity (BSCVA) at 12 months. The main analysis was to test that this proportion was > 0.50.

STUDY DESIGN DISCUSSION

The study design employed for the pivotal trial of the intraocular telescope, i.e., prospective, single-arm, multi-center, was appropriate for a number of reasons. First, a concurrent control arm was not required since the vision impairment in patients with stable severe (BCDVA of 20/80 or worse) to profound (BCDVA of 20/800 or better) caused by bilateral central scotomas associated with end-stage AMD is not reversible, and also not treatable.

The endpoint of improvement in visual acuity following implantation of the intraocular telescope is appropriate since vision is a well-established clinically relevant parameter, and widely used in clinical trials where improvement of visual acuity is the treatment goal. Similarly, evaluation of changes in the corneal endothelium represents a well-established safety parameter since the monolayer of corneal endothelial cells is responsible for maintaining the clarity of the cornea, allowing light to pass through unimpeded.

B. Accountability of PMA Cohort

For study IMT-002 196 (90%) of 217 enrolled patients were available for analysis for the 12-month visit and 174 (80%) for the 24-month visit. In study IMT-002-LTM, 85 patients were enrolled for the 36-month visit and 129 for the 48-month visit; 84 (99%) patients were available for analysis for the 36-month visit and 106 (82%) were available for the 48-month visit, and 84 (65%) returned for the 60-month visit.
Patient availability and accountability for Protocol IMT-002 are presented in Table 7 and for Protocol IMT-002-LTM in Table 8.

TABLE 7
AVAILABILITY AND ACCOUNTABILITY
OPERATED SUBJECTS (N = 217)
STUDY IMT-002

		1 Month	3 Months	6 Months	9 Months	12 Months	18 Months	24 Months
Available for Analysis	n/N (%)	217/217 (100.0%)	207/217 (95.4%)	204/217 (94.0%)	196/217 (90.3%)	196/217 (90.3%)	180/217 (82.9%)	174/217 (80.2%)
Discontinued	n/N (%)	0/217 (0.0%)	7/217 (3.2%)	11/217 (5.1%)	13/217 (6.0%)	16/217 (7.4%)	20/217 (9.2%)	29/217 (13.4%)
Deceased		0/217 (0.0%)	1/217 (0.5%)	3/217 (1.4%)	3/217 (1.4%)	5/217 (2.3%)	7/217 (3.2%)	10/217 (4.6%)
IMT removed postoperatively		0/217 (0.0%)	1/217 (0.5%)	1/217 (0.5%)	1/217 (0.5%)	2/217 (0.9%)	2/217 (0.9%)	8/217 (3.7%)
Lost to Follow-up	n/N (%)	0/217 (0.0%)	0/217 (0.0%)	0/217 (0.0%)	1/217 (0.5%)	2/217 (0.9%)	8/217 (3.7%)	13/217 (6.0%)
Missed Visit	n/N (%)	0/217 (0.0%)	3/217 (1.4%)	2/217 (0.9%)	7/217 (3.2%)	3/217 (1.4%)	9/217 (4.1%)	1/217 (0.5%)
% Accountability = Available for Analysis (Enrolled - Discontinued)		217/217 (100.0%)	207/210 (98.6%)	204/206 (99.0%)	196/204 (96.1%)	196/201 (97.5%)	180/197 (91.4%)	174/188 (92.6%)

TABLE 8
AVAILABILITY AND ACCOUNTABILITY
OPERATED SUBJECTS
STUDY IMT-002 –LTM

	30 Months	36 Months	42 Months	48 Months
Available for analysis	3/3 (100%)	84/85 (99%)	113/125 (90%)	106/129 (82%)
Discontinued (cumulative)			4/125 (3%)	6/129 (5%)
Deceased			3/125 (2%)	5/129 (3%)
IMT removed postoperatively			1/125 (1%)	1/129 (1%)
Lost to Follow-up			3/125 (2%)	10/129 (8%)
Missed Visit		1 /85 (1%)	5/125 (4%)	7/129 (5%)
% Accountability = Available for Analysis / (Enrolled - Discontinued)	3/3 100%	84/85 99%	113/121 93%	106/123 86%

Surgical complications led to 11 patients not being implanted with the intraocular telescope, leaving a cohort of 206 intraocular telescope-implanted patients. Table 10 shows the data for the eyes that were operated but did not receive the intraocular telescope. Of the 206 implanted eyes, 115 eyes were implanted with the WA 2.2X model device and 91 eyes were implanted with the WA 2.7X model device.

Of the 11 patients not successfully implanted, in 5 eyes the intraocular telescope was not implanted because of surgical complications and in 6 eyes intraocular telescope implantation was attempted but the device was removed at the time of surgery, also as a result of surgical complications. An intraocular lens was placed in these 11 eyes rather than the intraocular telescope.

TABLE 10
OPERATED EYES WITHOUT INTRAOCULAR TELESCOPE PLACEMENT
STUDY IMT-002

Number of Eyes	Surgical Complication
Cases with Intraoperative Contraindications for Intraocular Telescope Implantation	
3	Posterior Capsule Tear
2	Choroidal Detachment
Cases with Telescope Placed and Removed Intraoperatively	
4	Posterior Capsular Tear
1	Zonular Dehiscence
1	Choroidal Hemorrhage

C. Study Population Demographics and Baseline Parameters

The demographic characteristics at baseline are presented in Table 9 for operated patients in IMT-002. At baseline, mean age was 75.6 and mean BCDVA was 20/312.

TABLE 9
DEMOGRAPHIC AND BASELINE CHARACTERISTICS
OPERATED PATIENTS (N=217)
STUDY IMT-002

217 Eyes of 217 Operated Patients		
	Number	Percentage
Gender		
Female	103	47.5%
Male	114	52.5%
Age (In Years)		
Mean (SD)	75.6 (7.3)	
Anterior Chamber Depth		
Mean (SD)	3.15 (0.38)	
Minimum	2.48	
Maximum	4.74	

Type of AMD		
Geographic atrophy (GA)	85	39.2%
Disciform scar	93	42.9%
GA & Drusen	11	5.1%
GA & Disciform scar	8	3.7%
Drusen & Disciform scar	13	6.0%
GA & Drusen & Disciform scar	7	3.2%
Best-corrected Visual Acuity		
Mean BCDVA	20/312	
(Range)	(20/873, 20/80)	
Mean BCNVA @8"	20/315	
(Range)	(20/1262, 20/50)	
Mean BCNVA @16"	20/260	
(Range)	(20/632, 20/63)	

D. Safety and Effectiveness Results

1. Safety Results

Safety results from the intraocular telescope clinical trials, protocol IMT-002, a pivotal study, and protocol IMT-002-LTM, a long-term safety study in which patients implanted with the intraocular telescope under protocol IMT-002 were followed through 5 years, are discussed in this section.
The analysis of safety was based on subjects that had surgery for intraocular telescope implantation. Corneal endothelial cell density results, preservation of visual acuity, complications and adverse events are described below for the study population.

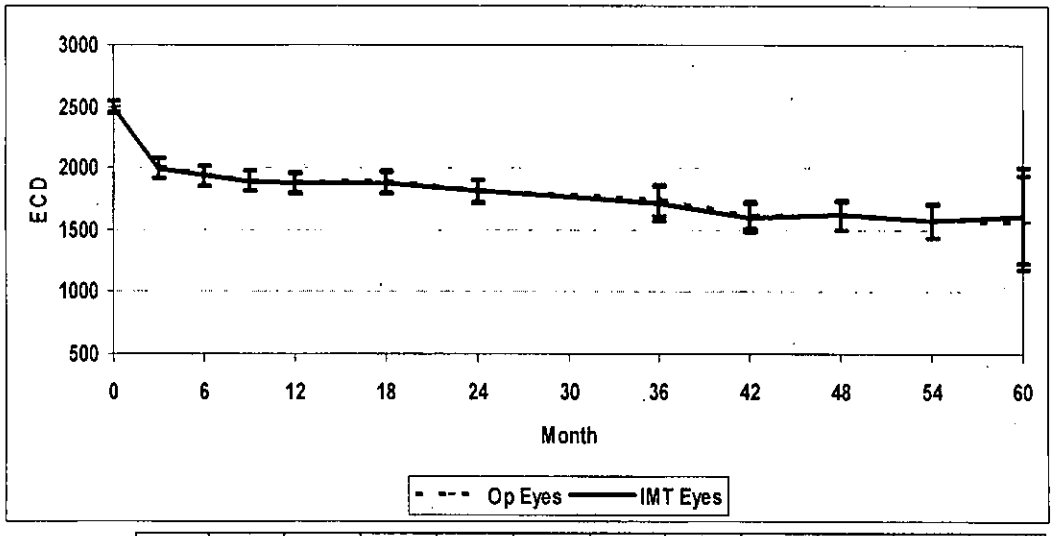
Corneal Endothelial Cell Density (ECD)

The IMT-002 protocol called for testing the hypothesis that population mean endothelial cell loss at one year did not exceed 17% in intraocular telescope implanted eyes. The mean ECD loss at 12 months was 25% (95% confidence interval 28% to 21%), thus failing to meet the ECD loss endpoint.

The most significant loss of corneal endothelial cells occurred from baseline to 3 months and from baseline to 6 months. This acute mean 20% (95% confidence interval 23%, 21%) ECD loss likely results from the 12 mm surgical incision required for insertion of the intraocular telescope, as well as the manipulation of the device during implantation. In the cohort of eyes with visits available at both 6 and 48 months (n=85), the mean annual ECD loss was approximately 3%. The mean rate of annual ECD loss estimated from all eyes across all time points (through 48 months) was 4.8% (see biexponential model discussion, page 24).

Figures 2 and 3 show the mean ECD and mean ECD percent change respectively over time for operated eyes and intraocular telescope implanted eyes. For intraocular telescope implanted eyes, mean ECD at baseline was 2496 cells/mm.^{2} At 3 and 6 months after implantation, mean ECD was 1995 cells/mm^2 and 1937 cells/mm^2 respectively; these changes in mean ECD translated into mean ECD percent loss from baseline of 20% and 22%, respectively. Mean ECD at 12 months after device implantation was 1871 cells/mm^2, a 25% loss from baseline. Mean ECD at 24, 36 and 48 months was 1808, 1713, and 1620 cells/mm^2, respectively, with associated mean percent losses of 28%, 31%, and 35%, respectively.

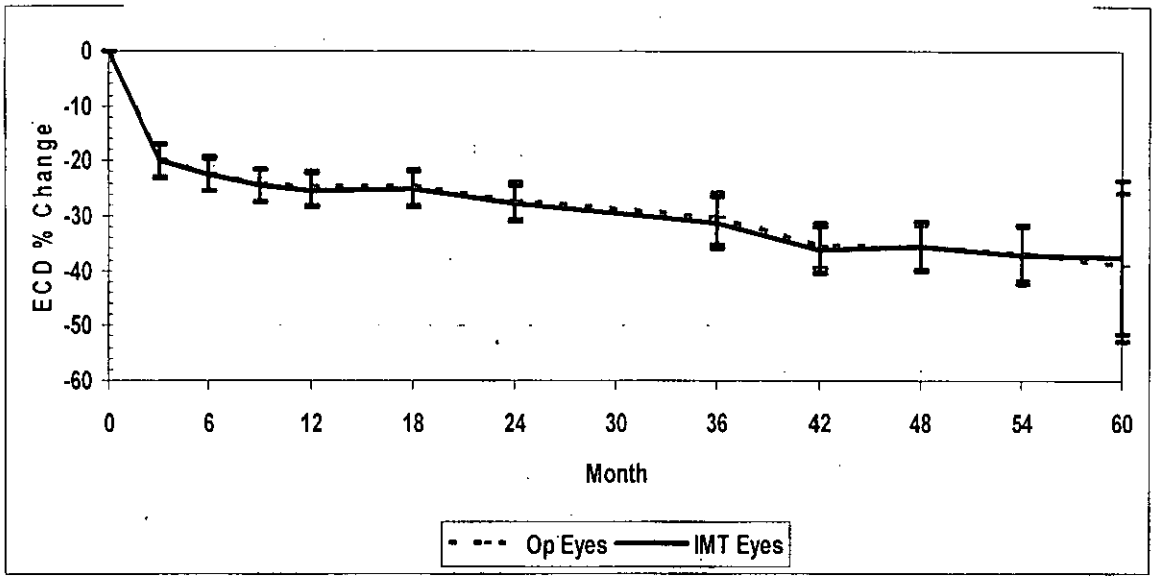
FIGURE 2
ECD (MEAN, CI)
OPERATED EYES AND INTRAOCULAR TELESCOPE-IMPLANTED EYES
STUDY IES IMT-002 AND IMT-002-LTM



		Preop	3 Months	6 Months	9 Months	12 Months	18 Months	24 Months	36 Months	42 Months	48 Months	54 Months	60 Months
Op Eyes	Mean	2498	2001	1936	1891	1881	1887	1813	1736	1612	1611	1572	1563
	95%CI	2451, 2546	1919, 2082	1855, 2016	1809, 1973	1795, 1967	1796, 1978	1723, 1903	1610, 1863	1505, 1720	1495, 1727	1439, 1706	1181, 1945
	N	216	198	200	190	190	182	173	79	110	94	65	18
	ECD<750	0 (0%)	6 (3%)	8 (4%)	9 (5%)	9 (5%)	13 (7%)	12 (7%)	3 (4%)	9 (8%)	7 (7%)	5 (8%)	3 (17%)
IMT Eyes	Mean	2496	1995	1937	1891	1871	1878	1808	1713	1595	1620	1572	1616
	95%CI	2447, 2545	1912, 2078	1856, 2018	1809, 1973	1786, 1957	1787, 1969	1718, 1898	1576, 1850	1481, 1709	1499, 1741	1431, 1713	1227, 2005
	N	206	193	198	190	186	180	171	70	101	88	60	17
	ECD<750	0 (0%)	6 (3%)	8 (4%)	9 (5%)	9 (5%)	13 (7%)	12 (7%)	3 (4%)	9 (9%)	7 (8%)	5 (8%)	2 (12%)

* ECD <750 – number and percent of eyes with ECD <750 cells/mm^2

FIGURE 3
ECD % CHANGE (MEAN, CI) FROM BASELINE
OPERATED EYES AND INTRAOCULAR TELESCOPE IMPLANTED EYES
STUDIES IMT-002 AND IMT-002-LTM



		Preop	3 Months	6 Months	9 Months	12 Months	18 Months	24 Months	36 Months	42 Months	48 Months	54 Months	60 Months
Op Eyes	Mean	0%	-20%	-22%	-24%	-25%	-25%	-27%	-30%	-35%	-36%	-37%	-39%
	95%CI		-23%, -17%	-25%, -20%	-27%, -21%	-28%, -22%	-28%, -21%	-31%, -24%	-35%, -26%	-40%, -31%	-40%, -32%	-42%, -32%	-53%, -26%
	N	216	198	200	190	190	182	173	79	110	94	65	18
IMT Eyes	Mean	0%	-20%	-22%	-24%	-25%	-25%	-28%	-31%	-36%	-35%	-37%	-38%
	95%CI		-23%, -17%	-25%, -19%	-27%, -21%	-28%, -22%	-28%, -22%	-31%, -24%	-36%, -26%	-40%, -32%	-40%, -31%	-43%, -32%	-51%, -24%
	N	206	193	198	190	186	180	171	70	101	88	60	17

Even patients who have baseline ECDs above the levels shown in Table 2 (page 2, Contraindications section) may experience low ECD leading to corneal edema if they have above average ECD losses at surgery, over time, or have longer than average life spans.

The range of ECD percent loss in intraocular telescope implanted eye is presented in Table 11.

TABLE 11
RANGE OF ECD PERCENT CHANGE FROM BASELINE
INTRAOCULAR TELESCOPE IMPLANTED EYE
STUDIES IMT-002 AND IMT-002-LTM

	3 Months	12 Months	24 Months	36 Months	48 Months	60 Months
Maximum Loss	-85%	-88%	-81%	-84%	-80%	-81%
95th Percentile	-67%	-69%	-75%	-69%	-74%	-81%
75th Percentile	-30%	-37%	-40%	-43%	-49%	-56%
50th Percentile	-13%	-21%	-24%	-28%	-36%	-40%
25th Percentile	-6%	-9%	-11%	-16%	-19%	-13%
5th Percentile	+6%	+1%	-0%	-5%	-6%	+2%
Minimum Loss	+18%	+13%	+28%	+11%	-2%	+2%
N	193	186	171	70	88	17

Negative sign (-) indicates decrease from baseline; positive sign (+) indicates and increase from baseline.

Table 12 summarizes the number of eyes with last measured ECD <1000, <750, and <500 cells/mm^2. At the patient's last available visit (which varied among patients), 31 of 206 eyes (15.0%) had ECD < 1000 cells/mm^2. This included a subset of 18 eyes (8.7%) with ECD < 750 cells/mm^2 and 7 eyes (3.4%) with ECD < 500 cells/mm.^{2} Limited numbers of patients were available for later visits. For the risk to the individual patient, please refer to the Kaplan-Meier analysis shown in Table 5.

TABLE 12
LAST AVAILABLE ECD < 1000, <750, <500 CELLS/MM^2
INTRAOCULAR TELESCOPE IMPLANTED EYES
(EXCLUDING RECORDS AFTER INTRAOCULAR TELESCOPE EXPLANTS AND CORNEAL TRANSPLANTS)
STUDIES IMT-002 AND IMT-002-LTM

ECD	N = 206		
	%	n/N	95% CI of %
ECD < 1000 cells/mm^2	15.0%	31/206	(10.5%, 20.7%)
ECD < 750 cells/mm^2	8.7%	18/206	(5.3%, 13.5%)
ECD < 500 cells/mm^2	3.4%	7/206	(1.4%, 6.9%)

In some eyes, ECD decreased to <750 cells/mm^2 in the early postsurgical period. In other eyes, ECD first decreased to this level later in the study period, up to and past 50 months postoperatively.

Patients should be advised of the potential risk of corneal edema leading to persistent vision-impairing corneal edema and the need for a corneal transplant due to loss of ECD resulting from surgery and further advised that ECD will continue to decline at a rate significantly higher than the 0.6% annual rate of ECD loss in phakic eyes.

While long-term ECD data is available as described above, to characterize the rate of mean annual ECD loss, a biexponential model (Predicting Endothelial Cell Loss and Long-Term Corneal Graft Survival, W. Armitage et al, *Investigative Ophthalmology and Visual Science*, August 2003, Vol. 44, No. 8) was developed to fit the ECD pattern from baseline to 48 months after intraocular telescope implantation. For all intraocular telescope implanted eyes the mean annual ECD loss was 4.8% (90% confidence interval 3.4%, 6.2%).

Using the biexponential model described above, Table 13 predicts the percentage of eyes with ECDs <1000, <750, and <500 cells/mm^2 through 60 months postoperative.

TABLE 13
PREDICTED PROBABILITY OF ECD LESS THAN THRESHOLD BASED ON BI-EXPONENTIAL MODEL FOR INTRAOCULAR TELESCOPE IMPLANTED EYES ENROLLED IN IMT-002 OR IMT-002-LTM STUDY BASED ON DATA FROM BASELINE TO 48 MONTHS (EXCLUDING PREOPERATIVE RESIDUALS)

Time	Probability of ECD		
	< 1000	< 750	< 500
3 Months	7.2%	2.8%	0.3%
12 Months	9.4%	5.0%	1.4%
24 Months	11.4%	6.7%	2.6%
36 Months	13.1%	8.2%	3.9%
48 Months	15.4%	9.6%	5.1%
54 Months	16.5%	10.4%	5.9%
60 Months	17.4%	11.4%	6.7%

The empirical frequency of residuals was used to estimate these probabilities.

There was no evidence from studies IMT-002 and IMT-002-LTM that rate of loss of ECD declined over time or that the rate of new cases of corneal edema declined.

When ECD levels fall too low (< 750mm^2), the cornea may become edematous, thicken and lose transparency, and corneal transplantation may be needed. The endothelial cell density needed to maintain corneal transparency is unknown and varies from patient to patient. Possible risk factors for endothelial cell loss are described in the following section.

Preservation of Visual Acuity

Protocol IMT-002 specified that preservation of visual acuity was to be assessed in terms of whether more than 10% of intraocular telescope-implanted eyes lost >2 lines of either BCDVA or best corrected near visual acuity (BCNVA) without a corresponding improvement in the other. This endpoint was met. At 12 months, 5% of eyes incurred such losses, and at 24 months, 6% of eyes incurred such losses.

At 36 months, 2 implanted eyes lost more than 2 lines of BCDVA, and 4 eyes (4.2%) lost more than 2 lines of BCDVA at 48 months. Six (6) eyes were seen at 60 months, and these eyes had no loss of BCDVA.

Over the 5-year period for studies IMT-002 and IMT-002-LTM, there were 15 cumulative reports of BCDVA loss of >2 lines from baseline at the last available visit.

Adverse effects that occurred in the PMA clinical study:

Ocular complications were defined as events directly related to the surgical procedure for intraocular telescope implantation, whether successful or not, occurring in the operative and immediate postoperative period. Events occurring after the immediate postoperative period were classified as adverse events. Ocular complications and ocular adverse events reported for the IMT-002 and IMT-002-LTM studies are shown in Tables 15 and 16 on the following pages, with the more serious events shown first in each table.

The intraocular telescope was not placed in 5 eyes due to surgical complications occurring prior to attempted implantation, primarily capsular rupture. The telescope was placed but removed intraoperatively in 6 eyes because of surgical complications (posterior capsule tear, zonular dehiscence, choroidal detachment). A standard intraocular lens was placed in these eyes.

Other significant ocular complications included corneal edema; iris damage and/or prolapse transillumination defects; and vitreous loss (Table 14).

The most common ocular complication was increased IOP requiring treatment $\leq$ 7 days (N = 59; 27.2%). (Increased IOP reported beyond 7 days and requiring treatment was classified as an adverse event, not as an ocular complication.) Increased IOP classified as an ocular complication was likely associated with the liberal use of high molecular weight viscoelastic material (Healon V) in the eye. Other commonly reported (occurring at a rate of 5% or greater) ocular complications were corneal edema, posterior capsular opacification, iris prolapse, and corneal abrasions. Fourteen (14) cases (6.5%) of corneal edema occurred within 30 days of surgery; all 14 cases were first reported on postoperative Day 1 and three of these cases of corneal edema were still noted at the 1 month visit. Posterior capsular opacification was reported for 13 eyes (6.0%); surgical capsulotomy was successfully performed in one patient. Iris prolapse was observed in 12 eyes (5.5%) and 11 eyes (5.1%) had corneal abrasions.

TABLE 14
OCULAR COMPLICATIONS, OPERATED EYES (N=217)
STUDIES IMT-002 AND IMT-002-LTM

Significant Ocular Complications	N	% (n/217)
Aborted surgery	5	2.3%
Choroidal detachment	2	0.9%
Choroidal hemorrhage	1	0.5%
Corneal edema ≤ 30 days after surgery	14	6.5%
Iris atrophy ≤ 7 days after surgery	4	1.8%
Iris damage	9	4.1%
Iris incarceration	3	1.4%
Iris prolapse	12	5.5%
Iris transillumination defects ≤ 21 days after surgery	8	3.7%
Phthisis	1	0.5%
Posterior capsular rupture	10	4.6%
Vitreous hemorrhage ≤ 7 days after surgery	1	0.5%
Vitreous in anterior chamber ≤ 7 days after surgery	3	1.4%
Vitreous loss	3	1.4%
Vitreous loss - vitrectomy required	7	3.2%
Other Ocular Complications		
Afferent pupil defect	1	0.5%
Alternating exotropia	1	0.5%
Anterior chamber hemorrhage	1	0.5%
Anterior segment neovascularization	1	0.5%
Anterior synechiae	3	1.4%
Asthenopia	1	0.5%
Bleb	1	0.5%
Blepharitis	7	3.2%
Blurred vision	1	0.5%
Chalazion	2	0.9%
Conjunctival injection	4	1.8%
Corneal abrasion	11	5.1%
Corneal endothelial touch	3	1.4%
Corneal neovascularization	1	0.5%
Cortical remnants	2	0.9%
Cyclitic membrane ≤ 7 days after surgery	1	0.5%
Cyclodialysis cleft	1	0.5%
Descemet's membrane separation	3	1.4%
Dry eye	1	0.5%
Ecchymoses on eyelid	1	0.5%
Ectropion	3	1.4%
Endothelial folds	2	0.9%
Epithelial basement membrane dystrophy	1	0.5%

Significant Ocular Complications	N	% (n/217)
Esotropia	1	0.5%
Exotropia	2	0.9%

TABLE 14 (CONTINUED)
OCULAR COMPLICATIONS, OPERATED EYES (N=217)
STUDIES IMT-002 AND IMT-002-LTM

Flashes	1	0.5%
Flat anterior chamber ≤ 21 days after surgery	2	0.9%
Folds in corneal graft	1	0.5%
Glare	1	0.5%
Glaucoma	1	0.5%
Haze	3	1.4%
Hyphema	10	4.6%
Hypotony	2	0.9%
Increased IOP requiring treatment ≤ 7 days after surgery	59	27.2%
Increased IOP ≤ 15 days after surgery	3	1.4%
Iridotomy ≤ 7 days after surgery	3	1.4%
Iritis ≤ 30 days after surgery	2	0.9%
Meibomian gland dysfunction	1	0.5%
Ophthalmic migraine	1	0.5%
Peribulbar hemorrhage	1	0.5%
Peripapillary hemorrhage	1	0.5%
Posterior capsule opacification	13	6.0%
Significant anterior chamber bleeding	3	1.4%
Strabismus	1	0.5%
Strabismus surgery	1	0.5%
Superficial punctate keratitis	2	0.9%
Surgical mydriasis	1	0.5%
Suture rupture	4	1.8%
Treatment of PCO	1	0.5%
Uveitis	1	0.5%
Uveitis/vitritis	1	0.5%
Vitreous bulge	1	0.5%
Watery eyes	3	1.4%
Worsening of subretinal scarring	1	0.5%
Wound leak	3	1.4%
Zonular dehiscence ≤ 7 days after surgery	1	0.5%
% = n/N ×100.		

Significant adverse events (Table 15) included persistent unresolved corneal edema (N=10, 4.6%), persistent vision-impairing corneal edema (N=8, 3.6%), corneal transplant

(N=5, 2.3%), and decrease in BCDVA (N=15, 6.9%). Device failures, dislocation and removal are also significant adverse events.

Adverse events occurring at an incidence of 5% or greater included deposits or precipitates on intraocular telescope (N=71; 32.75%), guttae (N=22; 10.1%), posterior synechiae (N=21; 9.7%), corneal edema (N=14; 6.5%), iritis (N=12; 5.5%), iris transillumination defects (N=12; 5.5%), intraocular telescope removal (N=12; 5.5%), and distorted pupil (N=11; 5.1%). In the majority of eyes, deposits/precipitates on the intraocular telescope resolved over the course of patient follow-up and did not affect visual acuity. Pigment and inflammatory deposits were managed medically with a standardized course of anti-inflammatory agents, starting with a sub-Tenon's injection of betamethasone depot administered at the end of surgery followed by topical administration of prednisolone acetate 1% or equivalent tapering over 2-3 months. All remaining adverse events in study IMT-002 were reported at a frequency of less than 5.0%.

There were no cases of endophthalmitis, retinal detachment, or retinal tear in the study population.

TABLE 15
OCULAR ADVERSE EVENTS, OPERATED EYES (N=217)
STUDIES IMT-002 AND IMT-002-LTM

Significant Adverse Events	**n**	**% (n/217)**
Choroidal neovascularization	5	2.3%
Corneal edema > 30 days after surgery *	14	6.5%
Corneal transplant (subset of persistent vision-impairing corneal edema)	5	2.3%
Decrease in BDCVA	15	6.9%
Device failure	2	0.9%
Endophthalmitis	0	0%
Iris atrophy > 7 days after surgery	9	4.1%
Iritis > 30 days after surgery	12	5.5%
Persistent unresolved corneal edema (subset of corneal edema) > 30 days after surgery)	10	4.6%
Persistent vision-impairing corneal edema (subset of persistent unresolved corneal edema)	8	3.6%
Retinal detachment	0	0%
Retinal tear	0	0%
Subretinal hemorrhage	6	2.8%
Telescope dislocation	4	1.8%
Telescope removal	12	5.5%
Vitreous hemorrhage > 7 days after surgery	3	1.4%
Vitreous in anterior chamber > 7 days after surgery	5	2.3%
Other Adverse Events		
Anterior chamber inflammation > 30 days after surgery	7	3.2%

Anterior ischemic optic neuropathy	1	0.5%
Cyclitic membrane > 7 days after surgery	1	0.5%
Cystoid macular edema	1	0.5%
Diplopia	4	1.8%
Distorted pupil	11	5.1%
Dry eye	10	4.6%
Entropion	2	0.9%
Exposed suture	3	1.4%
Eye pain	3	1.4%
Flat anterior chamber > 21 days after surgery	1	0.5%
Floaters	3	1.4%
Focal striae	2	0.9%
Foreign body sensation	9	4.1%
Guttae	22	10.1%

TABLE 15(CONTINUED)
OCULAR ADVERSE EVENTS , OPERATED EYES (N=217)
STUDIES IMT-002 AND IMT-002-LTM

Increased IOP requiring treatment > 7 days after surgery	8	3.7%
Inflammatory membrane	1	0.5%
Iridotomy > 7 days after surgery	3	1.4%
Iris transillumination defects > 21 days after surgery	12	5.5%
Obstructed iridectomy	1	0.5%
Ocular allergy	1	0.5%
Pigment epithelium around the peripheral iridectomy > 30 days after surgery	1	0.5%
Posterior synechiae	21	9.7%
Precipitates or deposits on intraocular telescope	71	32.7%
Ptosis	5	2.3%
Secondary glaucoma	2	0.9%
Subconjunctival hemorrhage	9	4.1%
Synechiae	1	0.5%
Tearing	1	0.5%
Visual disturbance	1	0.5%
Vitreous flare	1	0.5%
Zonular dehiscence > 7 days after surgery	1	0.5%

% = n/N ×100.

*Corneal edema reported in 13 intraocular telescope-implanted eyes and in 1 operated eye not implanted with an intraocular telescope

Corneal Edema

There were 14 (6.5%) intraocular telescope-implanted eyes with corneal edema >30 days after implantation surgery. There were 10 (4.6%) intraocular telescope-implanted eyes with persistent unresolved corneal edema at the last available visit. When ECD levels fall too low (< 750mm^2), the cornea may become edematous, thicken and lose transparency, and corneal transplantation may be needed. The endothelial cell density needed to maintain corneal transparency is unknown and varies from patient to patient.

Persistent vision-impairing corneal edema and Corneal Transplantation

Persistent vision-impairing corneal edema may require corneal transplant. There were 8 cases of persistent vision-impairing corneal edema in the study; 2 of these patients died without corneal transplant and 1 patient did not receive a transplant (reason unknown). Five (2.3%) study eyes underwent corneal transplantation in the IMT-002 and IMT-002-LTM studies. All 5 cases involved surgical complications at the time of intraocular telescope surgery. In 2 of the 5 cases, the intraocular telescope was removed during corneal transplantation procedure and replaced with an IOL. Visual acuity returned to baseline levels in these 2 patients. The intraocular telescope was left in place in the other 3 cases of corneal transplantation; the initial improvement in visual acuity from the IMT-002 study was retained in these eyes.

Choroidal Neovascularization

CNV was identified in one (1) eye in the IMT-002 study for an incidence of 0.5%, a rate consistent with that reported by Sunness et al., 1999.[1] An additional 4 cases of CNV were observed during the IMT-002-LTM study. These cases of CNV were successfully treated with thermal laser photocoagulation (Garfinkel et al, 2006)[2] photodynamic therapy or intravitreal injection of anti-VEGF therapeutic agents.

Device Failures, Removals and Replacements – Intraoperative and Postoperative

Table 16 summarizes the intraoperative and postoperative device failures, removals and replacements. Four device failures were reported in the IMT-002 study. Two of the intraocular telescope failures occurred during surgery and involved a broken haptic; one occurred before implantation and the device was not used, and one occurred during implantation, necessitating intraoperative replacement. The other 2 intraocular telescope failures involved condensation in the intraocular telescope portion of the device occurring one month postoperatively, resulting in device removal. No further device failures were reported over the course of follow-up through
4 years.

Intraoperatively, implantation of the intraocular telescope was attempted but unsuccessful in 6 eyes, as a result of surgical complications that included posterior capsule tear,

zonular dehiscence, and choroidal hemorrhage (Table 16). A standard intraocular lens was placed in these eyes.

Postoperatively, the intraocular telescope was removed from 12 eyes. Eight (8) subjects requested removal of the intraocular telescope because they were dissatisfied with the device. As noted above, the intraocular telescope was also removed from 2 eyes due to device failures and in 2 eyes that underwent corneal transplantation.

TABLE 16
INTRAOPERATIVE AND POSTOPERATIVE INTRAOCULAR TELESCOPE FAILURES REMOVALS AND REPLACEMENTS
STUDIES IMT-002 AND IMT-002-LTM

Intraoperative Removals (Number of Eyes)	
Broken Haptic	2*
Posterior Capsular Tear	4
Zonular Dehiscence	1
Choroidal Hemorrhage	1
Postoperative Removals Protocol IMT-002 and Protocol IMT-002-LTM (Number of Eyes)	
Condensation in the telescope portion of the intraocular telescope 1 month postoperatively	2
Dissatisfaction	8
Corneal Transplant	2

*1 broken haptic occurred before implantation

Table 17 provides ECD data for eyes that underwent postoperative intraocular telescope removal. In general, there was some ECD loss following intraocular telescope explanation, however there was considerable variability in the magnitude of loss. ECD loss was as high as 62%, but no lower than 13% in 6 eyes with data pre- and post-explantation.

TABLE 17
PREOPERATIVE & LAST AVAILABLE BCDVA AND ECD PRIOR TO & POST INTRAOCULAR TELESCOPE REMOVAL EYES THAT UNDERWENT POSTOPERATIVE INTRAOCULAR TELESCOPE REMOVAL (N = 12)
STUDIES IMT-002 AND IMT-002-LTM

PATIENT ID	MONTHS FROM DATE OF IMPLANT	PREOP BCDVA	LAST AVAILABLE BCDVA POST EXPLANT	ECD PRIOR TO EXPLANT CELLS/MM^2	ECD MOST RECENT VISIT POST EXPLANT CELLS/MM^2	COMMENTS
SUBJECT DISSATISFACTION						
001-XXX	31 Months	20/604	20/399	2544	1926	Patient dissatisfied
001-XXX	31 Months	20/551	20/726	1675	1454	Patient dissatisfied
004-XXX	22 Months	20/502	20/276	1772	666	Patient dissatisfied
008-XXX	10 Months	20/317)	20/289	1625	1100	Patient dissatisfied
008-XXX	12 Months	20/219	20/240	2891	2199	Patient dissatisfied
010-XXX	12 Months	20/381	NAV	1858	NAV	Patient dissatisfied
012-XXX	19 Months	20/276	20/166	2408	1389	Patient dissatisfied
020-XXX	41 Months	20/200	NAV	2258	NAV	Patient dissatisfied
DEVICE FAILURE OR CORNEAL TRANSPLANT						
013-XXX	1 Month	20/348	NAV	2316	NAV	Device failure
023-XXX	1 Month	20/348	20/458	2529	1234	Device failure
013-XXX	12 Months	20/303	20/348	463	1264*	Corneal transplant
031-XXX	08/10/2004	20/551	20/1002	385	1857*	Corneal transplant

NAV = not available.
*Post-PKP ECD

Other Secondary Surgical Interventions

Seven secondary surgical interventions not involving intraocular telescope removal were performed during the clinical studies. These procedures consisted of one YAG laser treatment of the anterior surface of the intraocular telescope to eliminate pigment deposits; 4 YAG laser peripheral iridotomies; one surgical repair of a distorted pupil; and one removal of a cortical fragment resulting from inadequate cataract removal.

2. Effectiveness Results

Effectiveness results from the intraocular telescope clinical trials, protocol IMT-002, a pivotal study and protocol IMT-002-LTM, a long-term safety study in which patients implanted with the intraocular telescope under protocol IMT-002 were followed through 5 years, are discussed in this section.

The intraocular telescope improved visual acuity and quality of life in most patients with end-stage macular degeneration. The primary effectiveness endpoint, a 2-line or greater gain in either distance or near best corrected visual acuity (BCVA) at 12 months in at least 50% of study patients, was met and exceeded. The secondary effectiveness endpoint, improvement in quality of life, was also achieved. The WA 2.7X device provided somewhat superior results as compared to the WA 2.2X, an outcome that would be expected given the higher magnification of this model.

Visual Acuity Primary Endpoint

Ninety percent (90%) of intraocular telescope-implanted eyes achieved at least a 2-line or greater gain in either distance or near BCVA at 12 months, thus exceeding the 50% criterion specified for the primary endpoint. This improvement was maintained at 24 months.

Change in BCDVA at 12 and 24 Months

Mean change in best corrected distance visual acuity was more than a 3-line improvement from baseline at both one and two years. At 12 months, 66% of patients had a gain of 3 or more lines of BCDVA, and 45% had a gain of 4 or more lines. Change in BCDVA from baseline is shown in Table 18.

TABLE 18
BCDVA CHANGE FROM BASELINE
ALL INTRAOCULAR TELESCOPE-IMPLANTED EYES
STUDIES IMT-002 AND IMT-002-LTM

	12 Months	24 Months	36 Months	48 Months	60 Months
	n (%)	n (%)	n (%)	n (%)	n (%)
N	193	173	74	96	6
Gain ≥ 6 lines	21 (10.9%)	16 (9.2%)	2 (2.7%)	7 (7.3%)	1 (16.7%)
Gain ≥ 5 lines	49 (25.4%)	33 (19.1%)	11 (14.9%)	9 (9.4%)	1 (16.7%)
Gain ≥ 4 lines	87 (45.1%)	74 (42.8%)	26 (35.1%)	27 (28.1%)	2 (33.3%)
Gain ≥ 3 lines	128 (66.3%)	103 (59.5%)	39 (52.7%)	46 (47.9%)	4 (66.7%)
Gain ≥ 2 lines	155 (80.3%)	129 (74.6%)	51 (68.9%)	65 (67.7%)	5 (83.3%)
Gain ≥ 1 line	170 (88.1%)	146 (84.4%)	63 (85.1%)	75 (78.1%)	5 (83.3%)
No change	19 (9.8%)	24 (13.9%)	9 (12.2%)	17 (17.7%)	1 (16.7%)
Loss > 2 lines	4 (2.1%)	3 (1.7%)	2 (2.7%)	4 (4.2%)	0 (0.0%)
Loss > 3 lines	3 (1.6%)	1 (0.6%)	2 (2.7%)	4 (4.2%)	0 (0.0%)
Loss > 4 lines	2 (1.0%)	1 (0.6%)	1 (1.4%)	4 (4.2%)	0 (0.0%)
Loss > 5 lines	2 (1.0%)	1 (0.6%)	0 (0.0%)	2 (2.1%)	0 (0.0%)
Loss > 6 lines	1 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean Change (SD)	3.43 lines (SD 2.31)	3.15 lines (SD 2.19)	2.74 lines (SD 2.17)	2.48 lines (SD 2.60)	3.57 lines (SD 2.74)

N = number of non-missing BCDVA change from baseline.

As shown in Table 19, mean BCDVA improved from 20/312 at baseline to 20/141 at 12 months and to 20/149 at 24 months. Mean BCNVA at 8 inches improved from 20/315 at baseline to 20/181 at 12 months and to 20/190 at 24 months. Mean BCNVA at 16 inches improved from 20/262 at baseline to 20/149 at 12 months and to 20/157 at 24 months.

TABLE 19
MEAN BCVA AT BASELINE, 12 MONTHS AND 24 MONTHS
INTRAOCULAR TELESCOPE-IMPLANTED EYES, STUDY IMT-002

	Baseline		12 Months		24 Months	
	N	Mean	N	Mean	N	Mean
Mean BCDVA 95% CI	206	**20/312** (20/334, 20/291)	193	**20/141** (20/152, 20/131)	173	**20/149** (20/161, 20/138)
Mean BCNVA at 8" 95% CI	206	**20/315** (20/341, 20/291)	192	**20/181** (20/196, 20/167)	173	**20/190** (20/207, 20/174)
Mean BCNVA at 16" 95% CI	206	**20/262** (20/282, 20/244)	192	**20/149** (20/161, 20/138)	173	**20/157** (20/170, 20/145)

Visual Acuity by Device Model

Improvements in BCDVA and BCNVA were achieved with both the WA 2.2X and WA 2.7X intraocular telescope models. A summary of improvement in visual acuity in terms of the primary effectiveness endpoint and percent of patients achieving at least a 2 and 3-line change are shown in Table 20.

TABLE 20
SUMMARY OF IMPROVEMENT IN VISUAL ACUITY
STRATIFIED BY INTRAOCULAR TELESCOPE MODEL, STUDY IMT-002

IMPROVEMENT IN VISUAL ACUITY	12 MONTHS		24 MONTHS	
	WA 2.2X	WA 2.7X	WA 2.2X	WA 2.7X
	% (n)	% (n)	% (n)	% (n)
≥2 LINES GAIN OF BCDVA *OR* BCNVA	89.0% (97)	91.6% (76)	84.5% (82)	88.2% (67)
BCDVA LINES GAINED				
≥3 LINES GAIN OF BCDVA	60.0% (66)	74.7% (62)	52.6% (51)	68.4% (52)
BCNVA LINES GAINED (8 OR 16 INCHES)				
≥3 LINES GAIN OF BCNVA	64.2% (70)	72.3% (60)	58.8% (57)	68.4% (52)

Long-Term Visual Acuity

Long-term follow-up data demonstrates that mean BCDVA improvements were generally retained over time in intraocular telescope-implanted eyes. There was a slight decline in BCDVA at 48 months (Table 21).

Table 21
MEAN BCDVA AT BASELINE, 12, 24, 36, 48, AND 60 MONTHS
INTRAOCULAR TELESCOPE IMPLANTED EYES
STUDIES IMT-002 AND IMT-002-LTM

BCDVA	Baseline	12 Months	24 Months	36 Months	48 Months	60 Months
Overall						
N	206	193	173	74	96	6
Mean 95% CI	**20/312** (20/334, 20/291)	**20/141** (20/152, 20/131)	**20/149** (20/161, 20/138)	**20/156** (20/175, 20/139)	**20/171** (20/191, 20/152)	**20/103** (20/228, 20/47)
WA 2.7X intraocular telescope						
N	91	83	76	29	37	4
Mean 95% CI	**20/326** (20/359, 20/297)	**20/127** (20/140, 20/115)	**20/141** (20/159, 20/125)	**20/157** (20/194, 20/127)	**20/170** (20/206, 20/140)	**20/118** (20/422, 20/33)
WA 2.2X intraocular telescope						
N	115	110	97	45	59	2
Mean 95% CI	**20/301** (20/331, 20/273)	**20/152** (20/169, 20/136)	**20/155** (20/172, 20/140)	**20/155** (20/179, 20/134)	**20/171** (20/198, 20/148)	**20/80** (20/2E5, 20/0)

Quality of Life

Quality of life, as assessed by the National Eye Institute's (NEI) Visual Function Questionnaire-25 (VFQ-25), was a secondary outcome measure. The VFQ-25 is a validated version of the NEI VFQ which measures vision-targeted health status for persons with chronic eye diseases including macular degeneration. A 5 point difference in subscale and/or composite scores may be interpreted as clinically significant. The VFQ-25 survey was administered at baseline and postoperatively. As shown in Table 22, implantation with the intraocular telescope improved quality of life in this study population.

VFQ-25 Results

Outcomes for all subscales of the VFQ-25 and the composite score are summarized in Table 23. At 12 months, the mean VFQ-25 composite score increased by a clinically significant amount (an increase of 6 points at 12 months). Overall, seven of the VFQ-25 subscales improved by clinically significant levels (general vision, near activities, distance activities, social functioning, mental health, role difficulties, and dependency). In subscales where no improvement or a decline in performance was expected (color vision, driving, and peripheral vision), performance was stable or declined. Also, the mean score of the general health subscale declined by 5 points, likely reflecting the impact of other health-related events on the non-vision related general health of the elderly study population.

TABLE 22
MEAN SCORE CHANGE AT 12 MONTHS
NEI 25-ITEM VISUAL FUNCTION QUESTIONNAIRE (VFQ-25)
INTRAOCULAR TELESCOPE IMPLANTED EYES
STUDY IMT-002

VFQ-25 Subscale	Preop Mean Score (95%CI) N = 206	12 Months Mean Score (95%CI) N = 193	Change from Preop Mean Score (95%CI) N = 193
General Vision	35.3 (33.2, 37.4)	50.3 (47.5, 53.1)	14.1 (11.0, 17.2)
Near Activities	25.5 (23.6, 27.5)	37.3 (34.6, 40.0)	11.2 (8.4, 13.9)
Distance Activities	34.3 (31.7, 36.8)	42.4 (39.1, 45.7)	7.9 (4.4, 11.4)
Color Vision	63.9 (60.1, 67.8)	67.7 (63.9, 71.5)	3.4 (-0.2, 6.9)
Social Functioning	49.3 (46.0, 52.7)	58.3 (55.1, 61.4)	8.6 (4.8, 12.4)
Mental Health	39.8 (36.5, 43.1)	49.3 (45.5, 53.0)	9.3 (6.1, 12.5)
Role Difficulties	37.4 (34.2, 40.7)	44.8 (41.0, 48.5)	7.3 (3.5, 11.0)
Dependency	37.7 (34.0, 41.4)	48.3 (44.4, 52.2)	10.0 (6.1, 13.9)
Ocular Pain	88.2 (86.0, 90.4)	88.5 (86.1, 90.9)	0.6 (-2.1, 3.3)
Driving	2.3 (1.0, 3.6)	1.9 (0.6, 3.2)	-0.5 (-1.6, 0.5)
Peripheral Vision	67.6 (63.9, 71.3)	62.9 (59.7, 66.1)	-5.9 (-10.4, -1.5)
Overall Composite	44.0 (42.1, 45.8)	50.3 (48.2, 52.4)	6.0 (4.0, 8.1)
General Health	64.0 (60.8, 67.1)	59.7 (56.4, 63.0)	-5.1 (-8.1, -2.0)

VFQ-25 scores on a scale of 0 (low) to 100 (maximum).
95%CI = 95% Confidence Interval.
General Health not included in Overall Composite per NEI VFQ-25 scoring guidelines.

The relationship between ≥ 2 line improvement in both distance and near BCVA and VFQ-25 overall composite score is shown in Table 24. In subjects that experienced a 2-line or greater improvement in both distance and near BCVA, 141 of 193 subjects (73%), the VFQ-25 mean composite score improved by a clinically significant 7.7 points at 12 months as compared to 2.4 points for subjects who did not experience that level of visual acuity improvement.

TABLE 23
RELATIONSHIP BETWEEN ≥ 2 LINE IMPROVEMENT IN BOTH DISTANCE AND NEAR BCVA IMPROVEMENT AND VFQ-25 SCORE COMPOSITE SCORE AT 12 MONTHS*
STUDY IMT-002

	N/%	Mean Change Composite Score
≥ 2 line improvement in both distance and near BCVA	141(73%)	+7.7
< 2 line improvement in both distance and near BCVA	52 (27%)	+2.4

*Hudson, et al, Implantable Miniature Telescope for the Treatment of Visual Acuity Loss Resulting from End-Stage Age-Related Macular Degeneration: 1-Year Results, Ophthalmology, Vol 113, Number 11, 2006

Since a 5-point change in the VFQ-25 may be interpreted as clinically significant, change in VFQ-25 composite score at 12 month from baseline is summarized in Table 24. At 12 months, 51.8% (100/193) of patients gained at least 5 points, while 25.9% (50/193) of patients reported no change (i.e., change within ± 5 points), and 22.3% of patients (43/193) lost at least 5 points in VFQ-25 composite score from baseline.

TABLE 24
12-MONTH VFQ-25 OVERALL COMPOSITE SCORE CHANGE FROM BASELINE
INTRAOCULAR TELESCOPE-IMPLANTED EYES AT 12 MONTHS
STUDY IMT-002

Change in VFQ-25 Composite Score	12 Months (N = 193)	
	%	n/N
Subjects with increase ≥ 5 points	51.8%	100/193
Subjects with change between -5 and 5 points	25.9%	50/193
Subjects with decrease ≥ 5 points	22.3%	43/193

As shown in Table 25, in subjects that gained 2-lines or more in BCDVA, 56% reported a clinically significant improvement in NEI-VFQ overall composite score. In subjects that had a < 2-line improvement in BCDVA, 37% reported a clinically significant improvement in NEI-VFQ overall composite score. 44% of subjects with a 2-line or more improvement in BCDVA did not report a clinically significant improvement in the overall composite score and 63% of subject that did not achieve a 2-line improvement in BCDVA did not report a clinically significant improvement in the overall composite score.

TABLE 25
RELATIONSHIP BETWEEN BCDVA CHANGE AND CLINICALLY SIGNIFICANT IMPROVEMENT IN VFQ OVERALL COMPOSITE SCORE AT 12 MONTHS
STUDY IMT-002

BCDVA Change from Baseline	VFQ Composite Score Change from Baseline		Total
	Clinically significant improvement (≥ 5 point increase)	No change or clinically significant decrease (< 5 point increase)	
≥2 line improvement	86/155 (55.5%)	69/155 (44.5%)	155/193 (80.3%)
<2 line improvement	14/38 (36.8%)	24/38 (63.2%)	38/193 (19.7%)
Total	100/193 (51.8%)	93/193 (48.2%)	193 (100%)

3. Subgroup Analysis

A number of possible risk factors associated with ECD loss, including presence of guttata in the eye, surgical specialty, and anterior chamber depth, were evaluated. Some possible risk factors are described in Table 26 below. These and other contraindications, precautions, and warning issues are discussed in the device labeling.

These potential risk factors were identified after the study, based upon inspection of the study data. They were not based upon testing protocol-defined hypotheses. This identification of risk factors is preliminary and not established by formal statistical testing. As a result, it is unclear how much, if at all, these factors may affect the loss of endothelial cells and associated rates of corneal edema.

TABLE 26
ENDOTHELIAL CELL DENSITY PERCENT LOSS — POSSIBLE RISK FACTORS
INTRAOCULAR TELESCOPE-IMPLANTED EYES
STUDIES IMT-002 AND IMT-002-LTM

	3 Months		12 Months		24 Months		36 Months		48 Months		60 Months	
	N	Mean	N	Mean	N	Mean	N	Mean	N	Mean	N	Mean
	95% CI		95% CI		95% CI		95% CI		95% CI		95% CI	
Intraocular Telescope-Implanted Eyes	193	**20%**	186	**25%**	171	**28%**	70	**31%**	88	**35%**	17	**38%**
	(17%, 23%)		(22%, 28%)		(24%, 31%)		(26%, 36%)		(31%, 40%)		(24%, 51%)	
Possible Risk Factors												
Guttata												
Not Present	167	**19%**	162	**24%**	150	**26%**	63	**31%**	76	**34%**	14	**33%**
	(16%, 22%)		(21%, 28%)		(23%, 30%)		(26%, 36%)		(29%, 39%)		(17%, 48%)	
Present	26	**26%**	24	**32%**	21	**36%**	7	**34%**	12	**44%**	3	**60%**
	(16%, 36%)		(22%, 42%)		(25%, 47%)		(20%, 47%)		(31%, 57%)		(7%, 100%)	
Surgeon Specialty												
Cornea Specialist	51	**13%**	52	**19%**	45	**20%**	18	**24%**	21	**25%**	3	**40%**
	(8%, 18%)		(14%, 24%)		(15%, 25%)		(17%, 30%)		(17%, 33%)		(-60%, 100%)	
Non-Cornea Specialist	142	**23%**	134	**28%**	126	**30%**	52	**34%**	67	**39%**	14	**37%**
	(19%, 26%)		(24%, 32%)		(26%, 34%)		(28%, 40%)		(34%, 44%)		(22%, 52%)	
Anterior Chamber Depth												
≥3 mm	116	**19%**	117	**25%**	106	**26%**	40	**29%**	50	**34%**	12	**36%**
	(15%, 22%)		(21%, 28%)		(22%, 30%)		(23%, 35%)		(28%, 40%)		(19%, 52%)	
<3 mm	77	**22%**	69	**26%**	65	**30%**	30	**34%**	38	**37%**	5	**42%**
	(17%, 27%)		(21%, 32%)		(24%, 36%)		(26%, 42%)		(30%, 45%)		(1%, 82%)	

Guttata

Corneal guttata has been shown to be a risk factor for endothelial cell loss following cataract surgery. The same risk may be present in intraocular telescope implantation surgery. The percent ECD loss at 3 months postoperatively was lower in non-guttata

eyes (mean loss 19%, 95% confidence interval 16%, 22%) than in eyes with guttata (mean loss 26%, 95% confidence interval 16%, 36%). Accordingly, the presence of guttata is a contraindication to the use of the intraocular telescope.

Surgeon Specialty

ECD loss at 3 months was lower for intraocular telescope implanted eyes operated by cornea specialists (mean loss 13%, 95% confidence interval 16%, 22%) than by non-cornea specialists (mean loss 23%, 95% confidence interval 19%, 26%). ("Cornea specialist" is defined as ophthalmologists who had fellowship or other specialty training in diseases and surgery of the cornea and who were at the time of the study regularly performing cornea surgical procedures such as penetrating keratoplasty.) Although the number of study subjects implanted by a cornea specialist is modest, there was lower ECD loss in these subjects of clinicians experienced in the medical management and surgical treatment of the cornea. Accordingly, there is a warning that only cornea specialists should implant the intraocular telescope. The long-term ECD data for intraocular telescope implantation performed by cornea specialists is based on limited data from a limited number of investigation sites.

Anterior Chamber Depth (ACD)

ACD $\geq$ 3.0 mm was associated with lower endothelial cell loss at 3 months postoperatively (mean loss 19%, 95% confidence interval 15%, 22%) as compare to patients with ACD < 3 mm (mean loss 22%, 95% confidence interval 17%, 27%). The finding of greater ECD loss in shallow anterior chambers (< 3.0 mm) at 3 months is likely the result of less working space in the anterior chamber and more surgical trauma to the corneal endothelial monolayer. Accordingly, the presence of an anterior chamber < 3.0 mm is a contraindication to the use of the intraocular telescope.

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

A. Panel Meeting Recommendation

At an advisory meeting held on July 14, 2006, the Ophthalmic Devices Panel recommended that the VisionCare Ophthalmic Technologies, Inc. PMA for the Implantable Miniature Telescope (by Dr. Isaac Lipshitz) be not approvable. The panel indicated that the data presented did not support the safety of the device. The FDA agreed with this recommendation and a not approvable letter was sent to the applicant on September 21, 2006. (http://www.fda.gov/ohrms/dockets/ac/06/transcripts/2006-4225t.pdf)

Longer term safety data collected and additional data analyses were performed by the applicant. Based on this additional data, FDA took this PMA to a second Ophthalmic Devices Panel meeting.

At an advisory meeting held on March 27, 2009, the Ophthalmic Devices Panel recommended that the VisionCare Ophthalmic Technologies,. Inc. PMA for the Implantable Miniature Telescope (by Dr. Isaac Lipshitz) be conditionally approved. The conditions were that survival analyses be completed to present long-term risk of corneal edema and corneal transplant to candidate patients and that two post-approval studies be conducted; one study will enroll and follow patients enrolled in study IMT-002 an additional 2 years to monitor safety, the other study will enroll patients under commercial conditions and follow patient 5 years to monitor the rates of surgical complications, vision-impairing corneal edema and corneal transplant.
(http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/OphthalmicDevicesPanel/ucm147051.htm)

B. FDA's Post-Panel Action

All panel recommendations are being implemented by VisionCare Ophthalmic Technologies, Inc.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL DATA

A. Safety Conclusions

Based on the clinical and non-clinical data available in the PMA, there is reasonable assurance of safety under the conditions of use prescribed, suggested, or recommended in the labeling. Even though the target criterion for the decrease in endothelial cell density endpoint was not met in the study, the modifications to the indications, along with the warnings and precautions regarding the use of this device, should mitigate the risks to a reasonable level.

B. Effectiveness Conclusions

The intraocular telescope implant has been shown to meaningfully improve visual acuity and improve the vision-related quality of life in patients with end-stage age-related macular degeneration. There is therefore reasonable assurance of effectiveness under the conditions of use prescribed, suggested, or recommended in the labeling.

C. 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. Given the limited options available to patients with endstage AMD, the benefits exceed the risks under the conditions of use prescribed, suggested, or recommended in the labeling.

XIII. CDRH DECISION

CDRH issued an approval order on July 1, 2010.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). The device is further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the device and insofar as the sale and distribution of the device are restricted to cornea specialists (an ophthalmologist who had fellowship or other specialty training in diseases and surgery of the cornea and who regularly performs corneal surgical procedures such as penetrating keratoplasty). FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at 2 years.

Continued approval of this PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. Two copies of this report, identified as "Annual Report" **(please use this title even if the specified interval is more frequent than one year)** and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the device, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes a complete protocol of your post-approval studies. Your PMA supplement should be clearly labeled as a "Post-Approval Study Protocol" and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm#2).

The applicant's manufacturing facility was inspected on May 6, 2010 and was found to be in compliance with the medical device Quality System (QS) regulation (21CFR 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 labeling.
Post-approval requirements and restrictions: See Approval Order.

XV. REFERENCES

[1]Sunness JS, Gonzalez-Baron J, Bressler NM, Hawkins B, Applegate CA. The development of choroidal neovascularization in eyes with the geographic atrophy form of age-related macular degeneration. Ophthalmol 1999;106:910-9.

[2]Garfinkel RA, Berinstein DM, Frantz R. Treatment of choroidal neovascularization through the Implantable Miniature Telescope. Am J Ophthalmol 2006;141:766-67.