The Argus II Implant is intended to be implanted in a single eye, typically the worse-seeing eye.

**CONTRAINDICATIONS**

- Ocular diseases or conditions that could prevent the success of the surgery (e.g. significant cataract, dry eye disease, central retinal artery or vein occlusion, history of retinal detachment, trauma, severe strabismus, etc.).
- Ocular structures or conditions that could prevent the successful implantation of the Argus II Implant or adequate healing from surgery (e.g. extremely thin conjunctiva, axial length <20.5 mm or >26 mm, corneal staphyomas, etc.).
- Ocular diseases or conditions (other than cataracts) that prevent adequate visualization of the inner structures of the eye (e.g. corneal opacity, etc.).
- Inability to tolerate general anesthesia or the recommended antibiotic and steroid regimen associated with the implantation surgery.
- Metabolic or active implantable device(s) (e.g., cochlear implant) in the head.
- Any disease or condition (e.g. significant cognitive decline, etc.) that prevents understanding or communication of informed consent, fitting of the Argus II System, or post-operative follow-up.

**PRECAUTIONS**

- In the event of any undesirable sensation when using the Argus II System (for example, immediately after operation of the system by removing the Argus II Glasses or turning off the Argus II VPU).
- The long-term effects of chronic electrical stimulation are unknown. Such effects may include deterioration of the retina or optic nerve. These effects may lead to deterioration of residual native vision and/or visual response to the Argus II System and could preclude subsequent replacement of the Argus II Implant with another retinal prosthesis system.
- Individuals with an Argus II Implant should only use a VPU that has been specifically programmed for them by their clinician or Second Sight personnel. Use of a different VPU may be ineffective in providing visual information and may cause physical discomfort or overstimulation.
- To avoid unwanted stimulation, do not use a VPU configured for Operating Room use for anything other than pre-implantation testing, testing during implantation, or during post-operative rehabilitation. Use of the Argus II System during or after such non-clinical situations may cause the patient to be detected on a resto-electric chart, which could preclude or change the way in which these stimuli are presented to the patient.
- Use of the Argus II System in the case of individuals who are severely hearing impaired, or have difficulty hearing, should be adequately communicated with the patient in order to program the Argus II System.
- Based on the spacing of the electrodes, the theoretical limit of resolution of the Argus II is 2.1 logMAR. However, in the clinical trial, one subject achieved a resolution better than this (i.e. 1.8 logMAR), likely due to head shadowing.
- Each Argus II implant has 60 electrodes, of which 55 are enabled. Up to 5 of the remaining 5 electrodes may be able to be enabled and programmed to replace an electrode if it fails post-implant.
- Persons should live within a distance of several feet from the scanner to temporarily relocate to a distance that will allow their full participation in recommended pre-operative clinical follow-up, device fitting, and training, and visual rehabilitation.

**REPORTED ADVERSE EVENTS**

A total of 30 subjects were implanted with Argus II in a clinical trial. An additional 16 patients (the Argus II 16 were implanted in Europe). Follow-up time ranged from 2.1 years to 4.6 years. At the time of the last report, each subject’s device was explanted at 1.2 years due to recurrent conjunctival erosion and refractory hypotony.

**Definition of Adverse Events**

In serious, adverse events (SAEs) were medically unexplained events or manifestations of disease, conditions, or complications that:
- Required medical or surgical intervention to prevent permanent impairment or dysfunction of a body function or permanent damage to a body structure.
- Caused permanent impairment of a body function or permanent damage to a body structure.
- Required hospitalization or prolonged hospitalization.

Events not meeting the above criteria were considered non-serious. All device-related or surgery-related events are summarized below.
Nineteen (19) subjects (83%) experienced no, or only non-serious, adverse events. These non-serious events were treated routinely with medicament or observation only. An additional 7 subjects experienced SAES that resolved with treatment or minor interventions.

The remaining 4 subjects were distinct from the other subjects in that they had a higher rate of adverse events due to a cascade of related events. In total, these 4 subjects accounted for 57% of all serious adverse events (SAEs) and 24% of all non-serious adverse events. Refer to Figure 1.

Figure 1: Overview of Safety Experience

Serious Adverse Events
Nineteen subjects did not have any device- or surgery-related serious adverse events (SAEs). Eleven subjects experienced a total of 23 device- or surgery-related SAEs (Refer to Table 1). Ten of the 23 events were considered to be related to the Argus II device and the remaining 13 were considered to be related to a surgical procedure. SAEs were generally treated with a surgical re-intervention(s) to link the device. This event eventually failed approximately 4 years post-implant, however, the device remained implanted.

Potential adverse events that did not meet the definition of an SAE were considered to be a non-serious adverse event. These events normally resolved on their own or were treated with medical management (i.e., they did not require surgical re-intervention to treat). There were 140 non-serious device- or surgery-related adverse events (in 28 subjects), of which 78 were device-related and the remaining 62 were surgery-related. The following non-serious events were reported (number of events is indicated in parentheses): ocular pain (17); conjunctival congestion (11), episternal membrane (11), elective revision surgery (7), non-serious conjunctival (7), subconjunctival (7), chlamydial (6), uveitis (6), inflammatory conjunctivitis (5), retinal thickening with cystoid macular edema (CME) (5), cutaneous infections (4), retinal thickening with no new cysts (4), vitreal hemorrhage (4), headache (3), high intracocular pressure (3), uveitis (3), retinal precipitates (3), corneal vascularization (2), epiphora (lacrimation) (2), and foreign body sensation (2). There was one reported case of each of the following events: 3 corneal edema, 5 corneal vascularization, 3 circumferential vitreous band traction, corneal edema, conjunctival cyst, retinal detachment, conjunctival edema, corneal abrasion, corneal dryness, corneal epithelial defect, corneal flaps, corneal fold, corneal subepithelial, decrease in visual acuity, fovea around the tack, filamentary keratitis, nausea, noptomastoius increase, ocular SAES, proliferative vitreous retinopathy, ptosis, serous retinal detachment, fractional retinal detachment, retinal folds, retinoschisis, subretinal, sub-conjunctival eyelashes, and vertigo.

Table 1: Serious Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th># of Subjects</th>
<th>% Subjects</th>
<th>Event</th>
<th># of Subjects</th>
<th>% Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjunctival desiccation</td>
<td>3</td>
<td>10.0%</td>
<td>Conjunctival erosion</td>
<td>3</td>
<td>10.0%</td>
</tr>
<tr>
<td>Corneal Melt - infective</td>
<td>1</td>
<td>3.3%</td>
<td>Corneal Opacity</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>Keratitis - infective</td>
<td>1</td>
<td>3.3%</td>
<td>Retinal detachment with no cystic ch</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>RD - retinomacular events</td>
<td>3</td>
<td>10.0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotony</td>
<td>4</td>
<td>13.3%</td>
<td>Corneal Melt</td>
<td>3</td>
<td>10.0%</td>
</tr>
<tr>
<td>Endophthalmitis - infective</td>
<td>3</td>
<td>10.0%</td>
<td>Retinal detachment</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>Keratitis - infective</td>
<td>1</td>
<td>3.3%</td>
<td>Intraocular inflammatory events</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>RD</td>
<td>2</td>
<td>6.7%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Surgical Re-Interventions

<table>
<thead>
<tr>
<th>Event</th>
<th># of Subjects</th>
<th>% Subjects</th>
<th>Event</th>
<th># of Subjects</th>
<th>% Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re-intervention to treat an AE</td>
<td>9</td>
<td>36.7%</td>
<td>Conjunctival repair</td>
<td>10</td>
<td>38.0%</td>
</tr>
<tr>
<td>Corneal shaping with EDTA</td>
<td>12</td>
<td>44.4%</td>
<td>Device explant</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>Device explant</td>
<td>1</td>
<td>3.3%</td>
<td>Re-tack</td>
<td>2</td>
<td>6.7%</td>
</tr>
<tr>
<td>Treatment of hypotony</td>
<td>4</td>
<td>6.7%</td>
<td>Laser - Retinal Tear</td>
<td>3</td>
<td>6.7%</td>
</tr>
<tr>
<td>Cross linking for corneal melt</td>
<td>4</td>
<td>13.3%</td>
<td>Elective revision surgery</td>
<td>7</td>
<td>23.3%</td>
</tr>
<tr>
<td>RD = retinal detachment</td>
<td>1</td>
<td>3.3%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Grating Visual Acuity

<table>
<thead>
<tr>
<th>Event</th>
<th># of Subjects Whose Grating Visual Acuity Improved</th>
<th>% Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>System ON</td>
<td>27% (n=8)</td>
<td></td>
</tr>
<tr>
<td>System OFF</td>
<td>0% (n=0)</td>
<td></td>
</tr>
<tr>
<td>Implanted Eye</td>
<td>3% (n=0)</td>
<td></td>
</tr>
</tbody>
</table>

Table 4: Door Task Results

<table>
<thead>
<tr>
<th>Event</th>
<th># of Subjects Whose Grating Visual Acuity Improved</th>
<th>% Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>System ON</td>
<td>27% (n=8)</td>
<td></td>
</tr>
<tr>
<td>System OFF</td>
<td>0% (n=0)</td>
<td></td>
</tr>
<tr>
<td>Implanted Eye</td>
<td>3% (n=0)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 2: Square Localization Results

- **Table**: Displays the observed mean accuracy within (5%) and (10%) visual angle intervals, respectively. The Argus II System was consistently performed better with the Argus II System vs. OFF or ON orientation and mobility tasks (finding a door and following a line, Figure 4 and Figure 5, respectively).
- **Figure**: Depicts the observed mean accuracy with the System ON and OFF over the course of the study. Figure 2 displays the observed mean accuracy which indicates the subject's mean distance from the center of the target square. Error bars represent the mean ± standard error.

On the Direction of Motion test, subjects were consistently able to perform better with the System ON versus System OFF over the course of the study. The Argus II System provided all 30 subjects with consistent results to the test.

During both the line and door tasks, subjects were only from subjects enrolled in 2009. Subjects enrolled in the study in 2007 and 2008 first performed this test at their 18th or 24th month follow-up visit. An assessment of Argus II subjects in and around their home by independent, certified low vision rehabilitation specialists was also performed. This assessment called the Functional Low-vision Observer Rated Assessment (FLORA) designed to evaluate how the Argus II System affected subjects’ wellbeing and functional vision. It was added to the

The Argus II System was added to study participants with benefit as measured by objectively-scored, partially-controlled functional vision tests. Subjects consistently performed better with the Argus II System in 2009. The Argus II System was added to study participants with benefit as measured by objectively-scored, partially-controlled functional vision tests. Subjects consistently performed better with the Argus II System in 2009. Subjects enrolled in the study in 2007 and 2008 first performed this test at their 18th or 24th month follow-up visit.
In non-clinical testing, the Argus II Implant produced the following temperature rise during MRI performed for 15-min of scanning (i.e., per pulse sequence) in a 3.3-Tesla (3-Tesla/128-MHz, Excite, HDx, Software 14X.M5, General Electric Healthcare, Milwaukee, WI) MR system: Highest temperature change was +2.1˚C.

Therefore, the MRI-related heating for the Argus II Implant at 3-Tesla using a transmit/receive RF body coil at an MR system settings was reported body averaged SAR of 3.9-W/kg indicated that the greatest amount of heating that occurred in association with these specific conditions was equal to or less than +2.1˚C.

Artfact Information
MRI image quality may be compromised if the area of interest is in the exact same area or relatively close to the position of the Argus II Implant. Therefore, optimization of MRI imaging parameters to compensate for the presence of the implant may be necessary.

MRI System
- Pulse Sequence: Imaging Plane
- Maximum Signal Void size - mm³

3-Tesla / 128 MHz (1.5-Tesla / 64MHz)
- TI-SE Parallel 0.39 (300)
- TI-SE Perpendicular 0.39 (300)
- GRE Parallel 2.54 (2440)
- GRE Perpendicular 3.81 (3600)

Device Functionality
The results of non-clinical tests indicated that the exposure of the Argus II Implant to various conditions using 1.5 Tesla/64MHz and 3.0 Tesla/128 MHz systems will not damage the device(s) or adversely affect the device’s functionality. However, it is strongly recommended that the Argus II Implant be handled by a qualified clinician or Second Sight personnel as soon as possible following an MRI procedure to confirm that it is still functioning properly.

STORAGE AND USE
Store the Argus II Implant at temperatures between -10° to 55° Centigrade (14° to 131° Fahrenheit).

Store the Argus II Externals (VPUs and glasses) at temperatures between 0° to 45° C (32° to 113° F). Only open the Argus II Externals at temperatures between 0° to 40° C (32° to 104° F).

HANDLING
The Argus II Implant packaging should be handled with care to avoid dropping, crushing, severe impact, and exposure to water.

SHELF LIFE
A “Use Before” date is located on the Argus II Implant packaging. This date is two years from the date of sterilization.

STERILIZATION
The Argus II Implant and Argus II spare Tacks are sterilized with indicators of sterilization. They are sterilized using ethylene oxide. Sterile packs should be carefully inspected to confirm that they have not been compromised. Sterility cannot be guaranteed if the sterile package is damaged or opened. These devices are for single-use only; do not re-stereilize or re-use them.

DIRECTIONS FOR USE & REQUIRED TRAINING
The following are the main steps required to use the Argus II System:
1. Device Implantation
2. Post-Operative Clinical Follow-Up
3. Device Fitting and Training
4. Vision Rehabilitation

In addition to this product insert, several manuals are provided with the Argus II System to provide more detailed instructions for use.

A Surgeon Manual, a video describing the surgical procedure and implantation of the Argus II Implant, and hands-on training are provided by Second Sight for all surgeons prior to implantation. The Surgeon Manual also includes instructional materials for Second Sight personnel and patients for eligibility for the Argus II System and provides a recommended clinical follow-up schedule. Surgeons must undergo this training in order to implant the Argus II Implant.

A Device Fitting Manual is provided to all clinical centers and is included with the Argus II Clinical Fitting System. The Device Fitting Manual provides instructions on how to use all components of the Argus II System. Physicians and/technicians must be knowledgeable about state-of-the-art Argus II System fitting procedures. These personnel must be fully trained and qualified by Second Sight in the fitting of the Argus II Implant.

A Patient Manual is provided in print and audio formats to all patients implanted with the Argus II Implant. The Patient Manual describes how to use the original equipment of the Argus II System that is provided to the patient. Argus II System recipients should receive training on all aspects covered in the Manual prior to taking the Argus II External Equipment home for everyday use.

A Visual Rehabilitation Guide and hands-on training is provided to low vision therapists who will provide visual rehabilitation training to Argus II patients post-implant.

For more information, contact Second Sight using the contact information provided on the front page of this insert.

INTELLECTUAL PROPERTY INFORMATION
Second Sight products (including the Argus II Retinal Prosthesis, Argus II Glasses, Argus II CDR Coil, Argus II Video Processing Unit and Argus II Clinical Fitting System) are covered by one or more of the following patents:

- United States: 5,109,844, 5,905,155, 5,944,747, 6,165,192, 6,507,758, 6,533,796, 6,718,209, 6,688,820, 6,920,358, 6,949,253, 6,974,333, 7,079,900, 7,007,775, 7,103,416, 7,127,286, 7,133,724, 7,142,909, 7,149,581, 7,181,287, 7,190,051, 7,211,103, 7,224,300, 7,228,191, 7,257,446, 7,263,493, 7,266,413, 7,291,540, 7,314,474, 7,318,522, 7,379,000, 7,480,986, 7,482,967, 7,463,750, 7,463,751, 7,453,169, 7,499,754, 7,527,621, 7,539,544, 7,565,202, 7,655,203, 7,571,004, 7,571,011, 7,574,263, 7,631,424, 7,638,032, 7,645,262, 7,666,523, 7,688,559, 7,687,774, 7,704,164, 7,704,163, 7,704,148, 7,794,911, 7,883,809, 7,891,799, 7,877,866, 7,835,798, 7,835,794, 7,816,914, 7,813,730, 7,776,197, 7,818,964, 7,765,009, 7,750,070, 7,749,608, 7,739,962, 7,734,352, 7,725,191, 7,709,961, 7,768,893, 7,691,252, 7,877,681, 7,900,010, 7,906,011, 7,912,556, 7,914,947, 7,905,305, 7,906,221, 7,977,513, 7,977,534, 7,975,810, 7,957,911, 7,962,221, 7,989,980, 7,951,476, 8,005,000, 8,010,200, 8,010,206, 8,014,866, 8,014,869, 8,014,879, 8,019,428, 8,024,229, 8,036,751, 8,036,752, 8,046,078, 8,060,211, 8,060,216, 8,068,913, 8,078,284, 8,085,062, 8,097,965, 8,093,313, 8,100,440.

- Australia: 2004235669, 2004255667, 2006200563, 2007021542, 2009204164, 7768797, 2004200105, 2006202583, 2002252113, 2002021497, 751995, 20032034174, 2003228959, 739523, 200606658, 200720658, 2006201464, 2006214142, 2006292220, 2006306660, 2006241404, 2007243163, 2007243164, 200725184, 2008311850, 2007208442.

- Europe: 11711188, 10619966, 10618752, 2197238.

- Japan: 43843634, 39265644, 4411088, 4206566, 3929701.

- Canada: 2,323,552, 2,323,551.

- Argentina, Second Sight and the Second Sight Logo are registered trademarks of Second Sight Medical Products, Inc. The accompanying material is copyright © 2012 Second Sight Medical Products, Inc. All rights reserved.