OIS @ASCRS

2ND ANNUAL
OPHTHALMOLOGY
INNOVATION
SUMMIT

April 18th, 2013 | The Westin Market Street, San Francisco, CA

OIS/ASCRS 2013 EXECUTIVE SUMMARY:

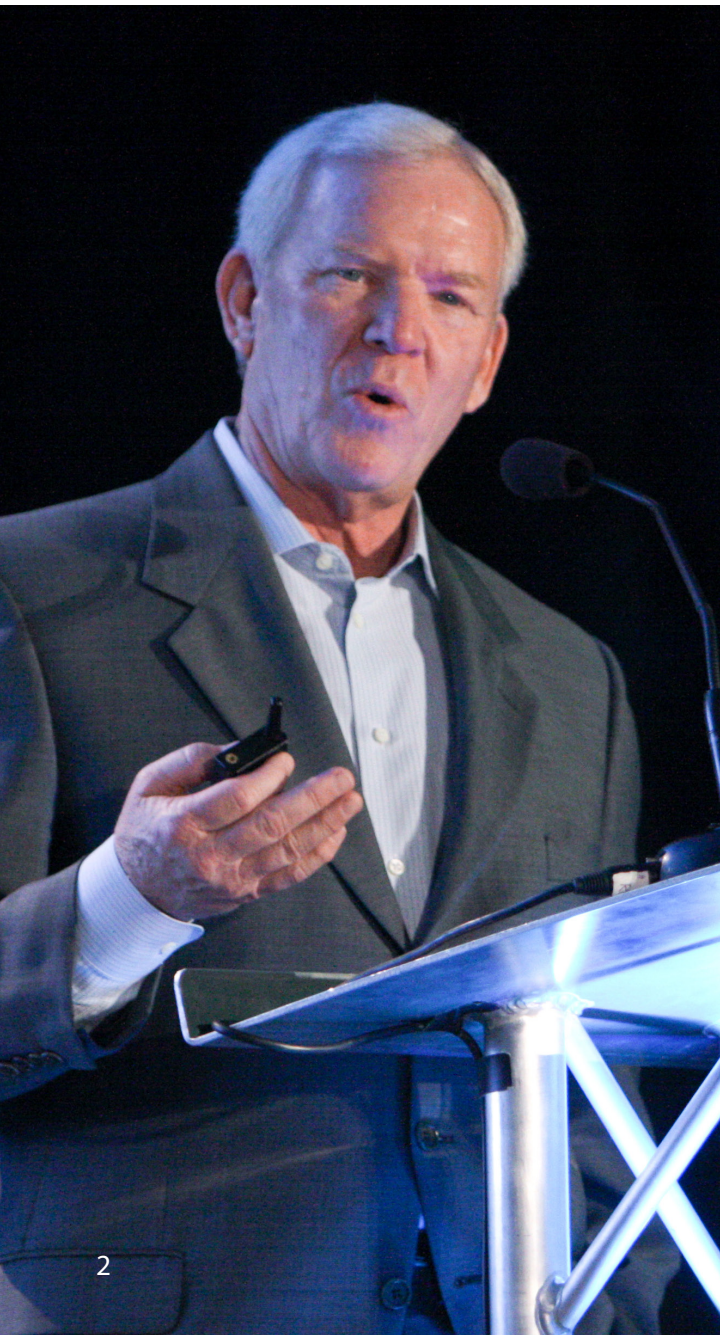
Eye on Innovation

OIS @ASCRS
OPHTHALMOLOGY INNOVATION SUMMIT

2ND ANNUAL OIS@ASCRS EXECUTIVE SUMMARY:

Eye on Innovation

By Michael Lachman



The Second Annual OIS@ASCRS—Ophthalmology Innovation Summit at the American Society of Cataract and Refractive Surgery—was held in San Francisco on April 18, 2013. The conference, produced by International Business Forum (IBF), attracted 325 attendees from 29 US states and 21 countries.

> **"OIS IS RESONATING because in the same room we're bringing together the inventors, the early adopting clinicians, the sources of capital and industry—those four constituencies that are required to power innovation."**
>
> ***— William J. Link, PhD, OIS Co-Chair and Managing Director, Versant Ventures***

NEW CATEGORIES OF OPHTHALMIC DEVICES have typically been pioneered by startup companies rather than by the established market leaders.

— Gil Kliman, MD, OIS Co-Chair and Managing Director, InterWest Partners

The purpose of OIS is to create an ecosystem of clinical, technology and business. Uniting this diverse group of key players in the ophthalmic field fosters innovation and facilitates business transactions. The conference provides a forum for addressing key issues impacting the ophthalmic field and a platform to showcase the most promising private ophthalmic companies. During this year's Summit, William J. Link, PhD, OIS Co-Chair and Managing Director, Versant Ventures, said, "OIS is resonating because in the same room we're bringing together the inventors, the early adopting clinicians, the sources of capital and industry—those four constituencies that are required to power innovation."

Key topics at the Summit included the funding of ophthalmic innovation, process improvements at the US Food and Drug Administration (FDA), as well as the emerging fields of refractive cataract surgery, presbyopia correction, and micro-invasive glaucoma surgery (MIGS).

The Fifth Annual OIS@AAO will be held on November 14, 2013 in New Orleans, just prior to the start of the American Academy of Ophthalmology Annual Meeting.

FUNDING OPHTHALMIC INNOVATION IN A CHALLENGING ENVIRONMENT

Bill Link began the meeting with a discussion of key trends in ophthalmic surgical innovation. Venture activity within the ophthalmic sector was minimal prior to the late 1990s, but since 1998 there have been VC

> **"IN OPHTHALMOLOGY TODAY, there is a very rapid pace of innovation that is going to cause a lot of discomfort to everybody—companies, regulators, and surgeons. I see the pace of innovation accelerating from here."**
>
> ***— Murthy V. Simhambhatla, PhD, President, Abott Medical Optics***

investments in over 50 ophthalmic start-ups. The venture funding backdrop for healthcare companies overall is "not a pretty picture" according to Link, with the number of initial venture deals declining 50% and initial venture investment dollars declining 64% between 2007 and 2012. However, said Link, "Innovation is directed where it is rewarded," and the market success of *Lucentis* for age-related macular degeneration (AMD) and *Restasis* for dry eye has attracted investment capital to these two segments. Link noted that there is now unprecedented alignment of

strong innovation in multiple ophthalmic surgical sectors, with innovation on the upswing simultaneously in cataract surgery (driven by premium IOLs, laser technology and intraoperative aberrometry), refractive surgery (driven by corneal inlays for presbyopia), and glaucoma surgery (driven by new micro-invasive devices).

Gil Kliman, MD, OIS Co-Chair and Managing Director, InterWest Partners, commented that new categories of ophthalmic devices have typically been pioneered by startup companies rather than by the established market leaders. Historical examples include excimer and femtosecond lasers for refractive surgery and accommodating IOLs; more recent examples include lasers for cataract surgery, micro-invasive glaucoma implants, intraoperative aberrometry and corneal inlays.

Murthy V. Simhambhatla, PhD, who brings experience in Abbott's vascular business to his current role as President of Abbott Medical Optics, observed "I see some remarkable parallels between the evolution of interventional cardiology and the evolution of cataract surgery." In ophthalmology today, "there is a very rapid

B+L IS WILLING TO ACQUIRE PRODUCTS THAT HELP PHYSICIANS address important clinical needs even if they represent limited financial opportunity.

— Calvin W. Roberts, MD, Chief Medical Officer, Bausch + Lomb

pace of innovation that is going to cause a lot of discomfort to everybody—companies, regulators, and surgeons. I see the pace of innovation accelerating from here."

Charles Warden, Managing Director, Versant Ventures, noted that with dramatically reduced availability of venture capital for early stage investment, many startups are having partnering discussions with large companies earlier in their development cycle. Renee Ryan, Vice President of Venture Investments at Johnson & Johnson Development Corp., has observed a similar trend within J&J, which historically has had a bias toward investing in companies with human data, but is now looking to get involved with companies at earlier stages.

Calvin W. Roberts, MD, Chief Medical Officer for Bausch + Lomb (B+L), pointed out that the company is focusing on the physician as an important source of innovation, as evidenced by partnerships with institutions such as the Bascom Palmer Eye Institute and the New York Eye and Ear Infirmary. Roberts said that B+L is willing to acquire products that help physicians address important clinical needs, even if they represent limited financial opportunity, citing as an example the 2010 acquisition of the orphan anti-viral drug *Zirgan*. Roberts also described the unusual situation in which an underperforming asset,

> **"THIS IS AN INCREDIBLE tool that becomes a blank canvas to work with as soon as you put it in the hands of innovators."**
>
> — ***Mark Forchette, CEO, OptiMedica***

the company's Technolas division, was spun out into a separately managed joint venture and was later reacquired after becoming an innovator in the field of laser cataract surgery.

FEMTOSECOND LASERS: EXPANDING THE MARKET FOR REFRACTIVE CATARACT SURGERY

The current era of refractive cataract surgery began during the middle part of the last decade, with the introduction of presbyopia-correcting and toric intraocular lenses (IOLs), and the Center for Medicare and Medicaid Services (CMS) ruling, that allowed patient self-pay for these refractive upgrades. Femtosecond (FS) lasers are seeing strong adoption and are expanding the definition of the premium channel in cataract surgery.

According to Stephen Slade, MD, who performed the first laser cataract procedure in the US, the global installed base of FS lasers for cataract surgery exceeds 400 (the actual number likely exceeds 500 at this time) in 52 countries, with 125,000 procedures performed, 2,000 surgeons trained and over 70 peer-reviewed publications. Novel imaging capability is a critical part of the value delivered by these lasers, and according to a CMS ruling issued late last year surgeons may bill patients for use of this imaging functionality when used to aid in the implantation of premium IOLs.

There are four high profile competitors in the FS laser cataract field. With the *LenSx* laser, Alcon (Novartis AG) has executed upon its first-to-market advantage to establish a clear market-leading share of installed lasers. Alcon has continued to improve the *LenSx* platform, with several important software upgrades and the new *SoftFit* Patient Interface, which was developed after the introduction of the laser to address important product issues, and to improve laser performance and clinical outcomes. The *Catalys Precision Laser System* from OptiMedica Corp. is a technology leading platform that was featured prominently in this year's ASCRS scientific program. *Catalys* clinical papers focused on successful treatment of challenging cataract cases and the ability to significantly reduce the amount of ultrasonic energy required for cataract removal, often completely eliminating the need for phacoemulsification. The *VICTUS* laser from B+L is positioned as a cost-effective combined platform for refractive surgery (LASIK flaps) and cataract surgery. The *LENSAR* cataract laser from LENSAR Inc. offers unique imaging technology and an "augmented
reality" system that generates an

accurate 3-D model of the eye.

Shareef Mahdavi of SM2 Strategic presented results of a recent survey covering over 200 US laser cataract surgeons operating at 65 centers. These centers are performing an average of 30% of their cataract procedures using the laser. With lasers now installed in centers that account for about 8% of all US cataract surgery volume, the 30% laser penetration in those centers suggests overall US procedure penetration of 2-3% at present. US surgeons are charging patients an average of $859 for use of the laser. Importantly, because of the astigmatism-correcting capabilities of the laser, nearly half of all current laser cataract procedures involve conventional instead of premium IOLs, and these conventional IOL cases are driving over 60% of incremental patient fees. Lasers covered in the survey averaged 57 procedures per month during Q1-2013, which is three-times the breakeven level of 19 per month based on actual costs for hardware, disposables and maintenance over a five year period.

> **“INTRAOPERATIVE ABERROMETRY has clearly been shown to improve patient outcomes.”**
>
> ***— Jack Holladay, MD***

Future applications of FS lasers were highlighted during a panel discussion. LENSAR CEO, Nick Curtis, reminded the audience that his company was originally formed to develop a laser that could soften the lens to restore accommodation, and added that LENSAR is still pursuing this goal. OptiMedica CEO, Mark Forchette,

mentioned new laser applications such as corneal transplants, new ways to correct astigmatism, lenticules for refractive correction, and micro-machining of the lens capsule and potential synergy with new IOL designs. Said Forchette, “This is an incredible tool that becomes a blank canvas to work with as soon as you put it in the hands of innovators.”

INTRAOPERATIVE ABERROMETRY: BRINGING NEW PRECISION TO REFRACTIVE CATARACT SURGERY

The other emerging technology for refractive cataract surgery highlighted at OIS was intraoperative aberrometry. These systems attach to the surgical microscope and provide on-demand intraoperative refractive measurements to assist surgeons with IOL power selection, toric IOL alignment and placement of astigmatism-correcting incisions. The market leader in this field is WaveTec Vision with its *Optiwave Refractive Analysis (ORA) System*. A competing system, *HOLOS IntraOp* from Clarity Medical Systems, could be available on a limited basis later this year.

At OIS, Jack Holladay, MD, a pioneer in the field of IOL power calculations, said, “Intraoperative aberrometry has clearly been shown to improve patient outcomes.” David Chang, MD, a leading cataract surgeon and President of ASCRS, added, “I think that intra-

“THE ULTIMATE IRONY would be if 15 years from now, everybody in this room has signed up for a refractive lens exchange with one of these accommodating adjustable IOLs, yet everyone is wearing Google Glasses to read their emails.”

— David Chang, MD, President of ASCRS

> **"I THINK THE LONG TERM SOLUTION IS going to be an electro-mechanical type of lens. The technology exists today, it just needs to get better."**
>
> ***— Eric Donnenfeld, MD, President-Elect of ASCRS***

operative aberrometry is very exciting, something that eventually every operating room will have. It's just a no-brainer to be able to, right there on the operating table, assess astigmatism and double-check the IOL."

Vance Thompson, MD noted that cataract surgery typically delivers refractive outcomes within 0.5 diopters of the target 60% of the time. The *ORA System* can achieve that level of accuracy 80% of the time, and WaveTec's new *VerifEye* system with continuous monitoring can achieve 84%. When *VerifEye* is combined with the femtosecond laser, refraction within 0.5D of target may be achieved 92% of the time, demonstrating the complementary nature of these two technologies. Dr. Slade commented, "Patients want LASIK-like results with their lens surgery," and noted that these visual outcomes look like they came from a LASIK trial.

On the difficult question of whether it is best for a surgeon to start with the FS laser or intraoperative aberrometry, Dr. Thompson said, "They go together, hand-in-hand, they're both critical, but if I had to choose one, I'd choose the aberrometer." Thompson highlighted the particular benefit of aberrometry in cataract patients that have had previous corneal laser vision correction surgery, in whom IOL calculations are particularly challenging.

Shareef Mahdavi presented survey

data covering over 100 users of the *ORA System*. For these surgeons, use of this technology has increased premium IOL penetration from 31% to 38%, reduced the LASIK enhancement rate from 10% to 5.3%, and generated an average of $337 per eye in incremental self-pay fees. These surgeons were using *ORA* not only in the 38% of cases involving premium IOLs, but in nearly 25% of their cases involving conventional IOLs as well. Said WaveTec CEO, Tom Frinzi, "The *ORA System* was reintroduced to the market 16 months ago. Since that time we've captured 2% of total cataract procedures and 10% of the premium market." Procedure penetration accelerated when the company transitioned from a per-procedure fee to a monthly subscription model.

CORNEAL INLAYS DRIVE THE NEXT WAVE OF SURGICAL PRESBYOPIA CORRECTION

Presbyopia is the condition in which an eye corrected for distance vision is unable to see at short distances due to age-related loss of accommodative ability. It is nearly universal after age 45, affecting 40% of the US population. Refractive surgery pioneer Richard L. Lindstrom, MD, founder of Minnesota Eye Consultants, said, "The surgical correction of presbyopia has been an interest of mine for decades. We have made much progress, but we have much progress yet

> **"THE SURGICAL CORRECTION OF PRESBYOPIA has been an interest of mine for decades. We have made much progress, but we have much progress yet to make."**
>
> ***— Richard L. Lindstrom, MD, Founder of Minnesota Eye Consultants***

THE MOST UNDERSERVED GLAUCOMA PATIENT POPULATION consists of the 60% of patients who are in the "middle class," taking two or more medications to address mild/moderate disease.

— Ike K. Ahmed, MD, University of Toronto

---

to make. Really what patients want to do is read. They don't necessarily care if they're accommodating, they want to overcome the handicap of needing glasses for reading." Eric Donnenfeld, MD, President-Elect of ASCRS, also noted that patients do not want to compromise their quality of vision in the process of reducing their dependence on glasses.

According to Dave Harmon of Market Scope LLC, presbyopia surgery represents a nearly $500 million global market today, consisting almost entirely of multifocal and accommodating IOLs. By 2017 the market could grow to $1.2 billion with the introduction of corneal inlays and other new products. At the "retail revenue" level, patient fees could grow from the current $2.4 billion to over $5 billion by 2017.

A number of different optical mechanisms are being employed in surgical presbyopia treatment. The most common surgical approaches in use today involve some form of monovision, in which one eye is corrected for distance vision and the other eye is

corrected for near vision. When the difference in correction is too large the patient can lose binocular fusion. Approximately 5-10% of patients do not neuroadapt well to monovision. Multifocal optics are the second most popular approach to presbyopia surgery worldwide, but they involve issues such as reduced contrast sensitivity and quality of vision, as well as night vision symptoms such as glare and halos.

Accommodating IOLs, which represent the third most popular approach to lens-based presbyopia surgery today led by *Crystalens* from B+L, are attractive because they restore the eye to its natural state and maintain excellent quality of vision. However, the key challenge with accommodating IOLs has been the ability to achieve sufficient amplitude of accommodation, which is ideally 3-5 diopters. Dr. Chang said that the *FluidVision* accommodating IOL under development by PowerVision Inc. "has huge potential. If you can get something like 4-6 diopters, you can overcome a little cylinder or a little macular degeneration. That would be truly awesome." Dr. Donnenfeld is less optimistic about achieving accommodation using forces inside the eye due to the many variables involved. He is the medical monitor for Elenza Inc., which is developing an accommodating IOL with battery powered liquid crystal optics. "I think the long term solution is going to be an electro-mechanical type of lens. The technology exists today, it just needs to get better. "

Presbyopia may also be addressed with surgical procedures performed on the cornea. Multifocal LASIK approaches have been marketed outside the US for many years, but have not seen widespread adoption. Two presby-LASIK treatments that have recently been made available outside the US, *SUPRACOR* from B+L Technolas and *PRESBYOND* from Carl Zeiss Meditec, involve more subtle blended optics and may prove to be more popular than earlier generations of multifocal laser treatment.

"Corneal inlays for presbyopia continue to make good progress," said Dr. Lindstrom. "This is the approach that I think is probably the most promising." Because not all patients adapt well to some of the optical approaches for treating presbyopia and because many surgical presbyopia patients will eventually require cataract surgery, removability is a key benefit of corneal inlays. There are three competing corneal inlay approaches under development and available outside the US, all of which are implanted in the

non-dominant eye, using a modified monovision approach to improve near vision. The *KAMRA* inlay from AcuFocus utilizes small aperture optics to create hyperfocality in the treated eye. The *Raindrop* inlay from ReVision Optics reshapes the anterior surface of the cornea to increase depth of focus. The *Flexivue Microlens* from Presbia is an intracorneal lens that boosts near vision via multifocal optics.

Dr. Chang closed the presbyopia panel discussion with this thought: “The ultimate irony would be if 15 years from now, everybody in this room has signed up for a refractive lens exchange with one of these accommodating adjustable IOLs, yet everyone is wearing Google Glasses to read their emails.”

OVER TIME COMPREHENSIVE OPHTHALMOLOGISTS, not just refractive surgeons and glaucoma specialists, will embrace MIGS technology.

— Kerry Solomon, MD of Carolina Eyecare Physicians

MIGS SHOWS PROGRESS ON MULTIPLE FRONTS

Micro-invasive glaucoma surgery, or MIGS, has emerged as an important new ophthalmic product category since the June 2012 FDA approval of the *iStent Trabecular Micro-Bypass Stent* from Glaukos Corp. The tiny

titanium device measures only 1mm in length and drains aqueous fluid from the anterior chamber into Schlemm's canal. It is approved for use during cataract surgery in the 20% of cataract patients that are treated with medications to reduce intraocular pressure (IOP), suggesting the potential for over 650,000 annual US procedures. Reimbursement codes and payment levels have been established that are favorable for both physicians and facilities.

Ike K. Ahmed, MD, who coined the term MIGS, said that the most under-

"WE HAVE BEEN LOOKING AT OUR PROCESSES, asking tough questions and trying to figure out what we can do to bring the innovation back to the US."

— Malvina Eydelman, MD, Director of the FDA Division of Ophthalmic and Ear, Nose, and Throat Devices

served glaucoma patient population consists of the 60% of patients who are in the “middle class,” taking two or more medications to address mild/moderate disease. Upstream of this group are the 30% of patients with early/mild disease that are well controlled with a single medication or a laser procedure, and downstream are the 10% with advanced disease that are candidates for more invasive trabeculectomy or tube shunt surgery.

> **“THIS IS A DEVICE THAT’S WORTH ALL OF THE EFFORT that the inventors and innovators have put into it.”**
>
> ***— Dean Lloyd, Second Sight - Argus II patient***

MIGS is defined as a very safe, minimally traumatic, conjuntiva sparing *ab-interno* procedure—performed through a clear corneal micro-incision under 2.0mm—with at least modest efficacy. The objective is to achieve IOP in the mid-teens and reduce medication use, while leaving the door open for more invasive surgical alternatives if required in the future. There are many companies working in parallel to develop alternative MIGS solutions that target three different outflow targets: Schlemm’s canal (which is the conventional outflow path and the target of the *iStent*), the suprachoroidal space, and the scleral/subconjunctival space.

MIGS devices under development with a Schlemm’s canal outflow target

include the *Hydrus Microstent* from Ivantis Inc. and the *iStent inject* from Glaukos. *Hydrus* is a flexible curved scaffold made from Nitinol that spans three clock-hours of the canal and gently dilates it, targeting multiple collector channels to reduce resistance to outflow. iVantis is currently enrolling its 558-patient US pivotal trial which combines *Hydrus* with cataract surgery. The *iStent inject* is one-sixth the size of the original *iStent*, facilitating the placement of two stents from a small gauge needle in a single pass. It has been shown clinically that two *iStents* provide better IOP lowering than a single *iStent.*

The *CyPass Micro-Stent* from Transcend Medical Inc. and the *iStent supra* from Glaukos are MIGS devices with outflow targets in the suprachoroidal space, which may provide superior drainage potential versus Schlemm's canal. *CyPass* is a biocompatible polyimide fenestrated stent measuring 6mm in length. Transcend recently completed enrollment of its US IDE clinical trial, which combines *CyPass* with cataract surgery in 505 subjects. The Glaukos *iStent supra* is 4mm device made from poly(ether sulfone) with a titanium tip.

The *XEN Glaucoma Implant* from AqueSys Inc. is a soft tissue-conforming gelatin device that is placed using a preloaded injector and shunts fluid to the subconjunctival space. AqueSys positions subconjunctival drainage as a "gold standard mechanism of action" because this is the same outflow target used in trabeculectomy. According to Dr. Ahmed, the subconjunctival drainage target creates a more potent potential IOP drop than the other two MIGS targets with a tradeoff of slightly greater risk profile. AqueSys is conducting an IDE clinical trial for its first indication.

Kerry Solomon, MD of Carolina Eyecare Physicians described how well MIGS fits into LASIK and refractive cataract practices that are built around enhancing patients' quality of life. Just as refractive vision correction may reduce dependence on glasses or contact lenses, MIGS can reduce a patient's dependence on topical glaucoma medications while potentially providing better control over the disease process. Over time, Solomon believes that comprehensive ophthalmologists, not just refractive surgeons and glaucoma specialists, will embrace MIGS technology. He is currently using *iStent* in 5% of his cataract cases; among his *iStent* patients that were on one medication pre-op, 88% were able to discontinue their drops post-op.

During the MIGS panel discussion,

glaucoma specialist Richard Lewis, MD, suggested that in the future MIGS could be offered to some patients as first-line treatment in order to avoid the compliance issues associated with eye drops. Tom Samuelson, MD noted that an even more immediate need is a broader label for *iStent* to enable US ophthalmologists to implant the device apart from cataract surgery. According to Glaukos CEO, Tom Burns, the company plans to work with the FDA to gain approval for expanded indications. Separately, the company is conducting studies to build a strong base of clinical evidence supporting use of the *iStent* in a broad range of non-cataract patients. Should payers decide to broaden the covered indications based on peer-reviewed studies, clinical usage could expand independently of the regulatory approval process.

REGULATORY PATHWAY: PROCESS IMPROVEMENTS AT THE FDA

Bill Link introduced Malvina Eydelman, MD, Director of the FDA Division of Ophthalmic and Ear, Nose, and Throat Devices, as someone who "has impacted nearly every ophthalmic device that's been approved or has aspired to be approved for well over the last decade." Dr. Eydelman reviewed the progress that the FDA has made over the past two years in reducing time it takes to reach approval decisions and improving the rate of positive decisions.

"The FDA staff is truly dedicated to bringing safe and effective devices in a timely fashion to the American people," said Eydelman. "We also believe that the US is and should remain the innovation leader. To that end we have been looking at our processes, asking tough questions and trying to figure out what we can do to bring the innovation back to the US." The FDA has drafted a guidance document that addresses clinical approaches in first-in-human trials, in an effort to bring more of this type of early stage clinical research back to the US.

One ophthalmic product segment that has been particularly challenging from a regulatory standpoint is premium IOLs. Eydleman believes that the primary cause of regulatory delays for these products is a lack of clarity on clinical endpoints. In order to address this issue, the FDA in collaboration with the AAO will hold a premium IOL workshop at the FDA campus on October 11, 2013. "I truly believe this is a game changer," said Eydelman. "Our goal is to present the challenges to ongoing innovation

with premium IOLs and to establish a basis for development of endpoints." The workshop will feature breakout sessions to encourage small group interaction among attendees from the FDA, industry and academia. One of the topics to be discussed will be a new class of premium IOLs that aim to deliver increased depth of focus.

FIRST OIS EYE ON INNOVATION AWARD PRESENTED TO SECOND SIGHT

In presenting the first OIS Eye on Innovation Award to Second Sight Medical Products Inc. and the company's CEO Robert Greenberg, MD, PhD, Bill Link commented, "How special is it if we can help blind people see? That's the power of this innovation."

The company's *Argus II* retinal prosthesis is the only approved treatment for severe retinitis pigmentosa, which affects 46,000 patients in the US and Europe. The product received the CE mark and was launched in Europe in 2011, and was approved by the FDA in February 2013. Over $200 million has been invested during a development timeline that has spanned more than 20 years—the first patent was filed in 1990. US reimbursement is pending and a US launch is slated for Q3-2013. With an ASP of $100,000, this initial indication alone represents a $4.5 billion market opportunity.

Dean Lloyd, an *Argus II* patient that was implanted with the device in 2007, was interviewed at OIS by his retinal surgeon and one of the inventors of the technology, Eugene de Juan, Jr., MD. Lloyd recounted his experience with the technology, concluding, "This is a device that's worth all of the effort that the inventors and innovators have put into it."

FOR MORE INFORMATION ON THE OIS MEETINGS, VISIT:

www.ophthalmologysummit.com
www.oisaao.com
www.oisascrs.com
www.oistv.net

This report was written by Michael Lachman, President of Lachman Consulting LLC, which provides strategic advisory and market research services to companies in ophthalmology and other medical technology fields.
www.lachmanconsulting.com

THIS REPORT WAS SPONSORED BY:

Abbott Medical Optics

Alcon®

REGENERON