OIS/AAO 2012 - EXECUTIVE SUMMARY

OIS @AAO

4TH ANNUAL
OPHTHALMOLOGY
INNOVATION
SUMMIT

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EYE ON INNOVATION

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4th Annual OIS Executive Summary: Eye on Innovation

By Michael Lachman

The Fourth Annual Ophthalmology Innovation Summit (OIS) was held in Chicago on November 8, 2012, just prior to the American Academy of Ophthalmology (AAO) Annual Joint Meeting. The conference, produced by International Business Forum (IBF), attracted a record 800+ attendees.

Hailing from 36 US states and 23 countries, the audience consisted of private ophthalmic company executives (43%), physicians/clinicians (19%), corporate/industry executives (18%), investment professionals (10%), service providers (5%) and press/media (5%).

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.

Presenting companies included 25 ophthalmic device and bio-pharma innovators at all stages of development, from early clinical to commercial. This year OIS added a session highlighting four companies in the rapidly evolving field of Health IT.

Panel discussions covered topics such as the latest FDA legislation and its impacts, emerging drug delivery technologies, the premium IOL market, pharmaceutical pipeline management and corporate leadership. Additional presentations addressed trends in ophthalmic venture capital and public market performance, the challenges facing corporate innovators and the impacts of the recent election on the industry.

The 2012 OIS was chaired by Emmett Cunningham Jr., MD, PhD, MPH, Partner, Clarus Ventures, LLC. Summit co-chairs were Gilbert Kliman, MD, Managing Director, InterWest Partners and William Link, PhD, Managing Director, Versant Ventures.

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Ophthalmology 2012: The Year in Review

"This is going to be a much bigger drug than people expect, perhaps the next billion dollar drug in ophthalmology."

-Emmett Cunningham Jr., MD, PhD, MPH
Partner at Clarus Ventures, LLC

OIS Chairman Emmett Cunningham Jr., MD, PhD, MPH, reviewed the key ophthalmic industry developments of the past year. There have been eight original ophthalmic NDA/BLA approvals over the past year, representing 6.8% of approvals across all medical segments. The first approval was for Eylea, from Regeneron Pharmaceuticals and Bayer in November 2011 for wet AMD. Eylea brings a dosing advantage to a market dominated by two Genentech anti-VEGF drugs, first-in-class Lucentis and low cost off-label Avastin. New drug delivery technology, some of which was presented at OIS, has the potential to radically alter the AMD landscape. Combination therapy may also take wet AMD treatment to the next level, with encouraging Phase 2b results from Ophthotech earlier this year for anti-PDGF therapy combined with anti-VEGF.

There have also been significant product approvals over the past year for previously untreated indications. In August, Lucentis became the first drug approved for DME. ThromboGenics received FDA approval for JETREA for symptomatic vitreomacular adhesions (VMA). "This is going to be a much bigger drug than people expect, perhaps the next billion dollar drug in ophthalmology," according to Cunningham.

On the device side, there have been two original PMA approvals over the past year. "Far and away, the most significant advance has been the validation of minimally invasive glaucoma surgery, or MIGS, with the approval of Glaucos' iStent," said Cunningham. Market Scope expects the number of MIGS procedures to surpass traditional filtering and shunt procedures for glaucoma by 2015.

The Ophthalmology Market: A View from the Public Sector

Anthony Gibney, Managing Director at Leerink Swann, presented an overview of public ophthalmic company stock performance and M&A trends. 2012 has been the best year for biotech stock performance since 1999. The AMEX Biotechnology Index has risen 39% over the past year, versus 19% for the S&P 500. Medical device stocks have lagged biotech, but have still had a year of very substantial growth. Gibney attributed this broad based performance to several factors, including confidence in company execution, increased expectation of M&A and higher predictability of regulatory agencies.

Eye stocks have kept pace, led by Regeneron. The company's $10 billion increase in market capitalization exceeds the $7 billion of venture capital that was invested in all of healthcare over the past 12 months. The market cap of ThromboGenics has doubled to nearly $2 billion over the same period.

The overall projected revenue growth for ophthalmic pharmaceuticals between 2011 and 2017 is an "anemic" 4% annually, from $10.1 billion to $12.7 billion, impacted significantly by genericization of key drugs. However, Gibney sees upside to this scenario. "This trend substantially underestimates the reality that breakthroughs in some of the other indications, that so far have not been treatable, are not in these numbers. **Analysts do not forecast what they don't see clinically, so breakthroughs in Phase 2 and Phase 3 over the next couple of years could fully double the growth rate."**

With respect to M&A, 2012 has been a quieter year than 2011 within ophthalmology. However, this has been offset by a substantial increase in licensing activity over the past year. For public financing, 2012 has been "a bit of an off year" as well. Of the over 15 biopharma and device IPOs in 2012, none were in ophthalmology. But Gibney expects more public funding activity in 2013, including one or two "substantial" ophthalmic IPOs, driven by positive developments announced over the past six months.

Private Funding and Exit Trends in Life Sciences

Jonathan Norris, Managing Director of SVB Capital, part of Silicon Valley Bank, reviewed trends in venture capital and private company exits. Norris expects that total venture investment in 2012 will remain at the same $28 billion level seen in 2011, but that the percentage of dollars invested in life science companies will fall to 18-20% of the total. This is well below the 26-30% trend seen over the past eight years and the lowest percentage since 2001, resulting in total life science VC investment of $5.0-$5.5 billion for 2012; Norris expects $4-5 billion of life science VC investment per year over the next couple of years.

Norris described a life science "funding gap" - although there has been about $19 billion in life science VC investment over the past three years, only about $7.5 billion has been raised over the same period. This overfunding has created a bottleneck. Over the past 12 years, $38 billion has been invested in over 2,600 life science companies that are still private. **"This backlog is going to take 10-12 years to get through, looking at the current pace of exits."** While this is a problem, it also represents an opportunity for funds with fresh capital to deploy in older companies that have mitigated risks and attractive valuations.

Between 2005 and 2011, ophthalmology was the fourth largest area for life science venture investment, with over $1 billion invested. Ophthalmology companies, both biotech and medical device, have been among the most capital intensive, ranking at or near the top in dollars raised per company. Among medical device company exits since 2005, ophthalmology has been one of the best performing sectors with respect to both returns on invested capital and time to exit, while investment returns in ophthalmic biotech have lagged behind other sectors.

Keynote Lectures:

Industry Leaders Discuss Challenges Facing Ophthalmic Innovators

Scott M. Whitcup, MD, Executive Vice President of R&D and Chief Scientific Officer of Allergan, Inc., was presented with the 2012 OIS "Road to Success" Award. In a presentation "Innovation in Ophthalmology: Beauty is in the Eye of the Shareholder,™" Whitcup addressed industry challenges such as increasing development costs and regulatory hurdles which have made it harder to innovate. In particular, companies have to prove that new therapies are not just effective but better than existing therapies, many of which are going generic. Whitcup drew an analogy of every new song having to be better than the existing Beatles portfolio. Drug developers are beginning as early as Phase 2 to generate cost effectiveness data in addition to safety and efficacy data.

Whitcup outlined several reasons why **"Ophthalmology is still a great place to be, where the glass is more than half full."**

- People care a great deal about their vision
- Favorable demographics: The population is aging and many eye diseases are age-related
- Eye care drugs and devices can be sold with relatively small specialty sales forces, so not every product has to be a blockbuster to succeed
- There are many conditions with unmet medical needs, such as dry AMD and presbyopia
- Many eye therapies are applied locally, avoiding safety and delivery issues associated with systemic therapies and allowing for "innovative repurposing" of systemic drugs from other fields
- Ophthalmology also includes self-pay consumer opportunities that avoid reimbursement issues

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Kevin Buehler, Division Head of the Alcon business unit of Novartis, followed Dr. Whitcup with a presentation entitled, “Unmet Medical Needs in Ophthalmology and Innovation Deliverables,” and pointed out up-front that the two talks shared similar themes. Buehler noted, “The world is clearly changing and if we continue to operate the way we’ve operated for the last 15 years going forward, it will not work. When we think about innovation, we can’t think of it simply in the context of new products; we need to think about it in the environment that we are working in.”

Buehler characterized the level of unmet medical need within ophthalmology as a 6 or 7 out of 10, while payer willingness to pay for new technology is closer to 3 out of 10 and probably declining. This raises the bar for new technology and makes innovation increasingly challenging. On the positive side, patients’ interest in protecting their vision is very high and should not be underestimated. If the payer was out of the way and patients could be asked directly if the clinical benefit of technology is worth the cost, this would represent a tremendous opportunity for innovation within the ophthalmic industry.

In today’s environment, Alcon is requiring even early stage business development partnerships to have progressed past the idea/proof-of-concept stage to include also a sound clinical data plan, initial safety package, stable product design, simple payer rationale and intellectual property approach.

Panel: Impact of the Latest FDA Legislation on Industry, VCs and the FDA Itself

-William J. Link, Ph.D., Managing Director, Versant Ventures
-Wiley Chambers, M.D., Supervisory Medical Officer , Division of Transplant and Ophthalmology Products in the Center for Drug Evaluation and Research at the Food and Drug Administration (FDA)
-Edward Peterson, President and CEO, AcuFocus
-Quinton Oswald, CEO, SARcode Bioscience
-Malvina B. Eydelman, M.D., Director, Division of Ophthalmic, Neurologic and Ear, Nose and Throat Devices Office of Device Evaluation, Center of Devices and Radiological Health
-Richard L. Lindstrom, M.D., Founder & Attending Surgeon, Minnesota Eye Consultants

Richard Lindstrom, MD, Founder and Attending Surgeon, Minnesota Eye Consultants, began this session by reviewing the key provisions of the FDA Safety and Innovation Act (FDASIA), which passed into law in July 2012, consisting of the third re-authorization of the Medical Device User Fee Act (MDUFA III) and the fifth re-authorization of the Prescription Drug User Fee Act (PDUFA V). Under MDUFA and PDUFA, the FDA can collect user fees from industry that, according to Lindstrom, "should allow the FDA to recruit, retain and motivate more good people to allow our regulatory process to function." In exchange for this funding the FDA has committed to meet certain performance goals and has "agreed to become more transparent, more efficient and more available," said Lindstrom.

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The industry and VC panelists agreed with Lindstrom's contention that more predictable, transparent regulatory processes and more timely approvals would attract greater investment into ophthalmology, creating innovative new products. Said Lindstrom, **"We think of [the FDA] as the problem, but they really are the solution."**

Malvina B. Eydelman, MD, Director of FDA's division of Ophthalmic, Neurologic and ENT Devices, said that these acts will have a "tremendous impact" on the FDA's medical device staffing, infrastructure and regulatory process. At OIS, Eydelman announced that her division had recently undergone reorganization, splitting ophthalmic and ENT devices from neurological and physical medicine devices. "As you can imagine, I'm very excited about this and I really think it's a huge step forward for ophthalmic devices."

Wiley Chambers, MD, Supervisory Medical Officer, FDA's Division of Transplant and Ophthalmology Products, noted that his staff devoted to ophthalmology has actually decreased in number in recent years.

Ed Peterson, President and CEO of AcuFocus has been working toward FDA approval of an intra-corneal inlay product for a number of years. He noted that face-to-face meetings with the FDA have been productive. **"Our relationship with the FDA, in the meetings, has been helpful, has been directive and has worked well."** Peterson added, "I think the only issue that all of us have had is timelines to get back together."

CEO Quinton Oswald, of SARcode Bioscience, echoed Peterson's observation that the time it takes to schedule follow-up meetings is an issue. Oswald also commented, "Uncertainty in a startup is the kiss of death" and regulatory risk is a major source of uncertainty. Having said that, Oswald followed, **"We've found the FDA very open and very clear in its direction to us."**

The FDA's Chambers closed with the following bit of advice for industry: **"The biggest message I tell people is not to spend lots of time debating what you think we might think about something, but to ask. You may not like the answer, but instead of spending time trying to guess what we're thinking, we usually can answer fairly quickly."**

Device Panel: The Outlook for Emerging Drug Delivery Technologies

K. Angela Macfarlane, President and CEO of ForSight Labs, moderated a panel showcasing three examples of ophthalmic drug delivery technology and addressed issues related to development, reimbursement and the outlook for the future. According to Macfarlane, **"Ophthalmology is unique in that it has a history of approval of drug delivery devices and implants."** Prior to OIS, Macfarlane obtained feedback from opinion-leading physicians indicating that the demand for new methods of ophthalmic drug delivery is driven primarily by the need to reduce the high treatment burden and low compliance associated with chronic medications. Drug delivery technology may also enable new therapies that would not be deliverable using traditional methods.

Ted Danse, President and CEO of Neurotech, reviewed his company's "powerful and truly transformational" Encapsulated Cell Therapy (ECT) technology platform for long-term recombinant protein delivery for retinal disease. Human retinal pigment epithelial (RPE) cells are engineered to over-express a specific protein of interest and the cells are encapsulated in a semi-permeable hollow fiber membrane, which is implanted in the back of the eye for multi-year delivery. Neurotech is in Phase 2 development for indications including wet AMD and a number of orphan diseases.

Sue Washer, President and CEO of AGTC, noted that AGTC is a gene therapy company that would not typically be represented on a medical device panel. The company's drug delivery technology uses naturally occurring viruses to deliver a therapeutic product to the back of the eye. AGTC is looking mostly at orphan indications - diseases that cause blindness at very young ages due to genetic deficiencies in millions of people globally. Five years of human data and ten years of animal data have demonstrated long-term delivery from a single injection.

Signe R. Erickson, PhD, VP of Development at ForSight Vision4, made the first public presentation of this company's technology a refillable, durable intraocular implant for sustained drug delivery in the vitreous. Following a single surgical implantation procedure, the device may be refilled periodically in a proprietary minimally invasive procedure. The goal is to make this a robust platform for small molecule and large molecule/biologic drugs. The company has demonstrated proof-of-concept with the completion of Phase 1 for wet AMD with sustained delivery of Lucentis, in collaboration with Genentech.

Erickson and Danse noted that retinal physicians are comfortable with surgical procedures, so the need for implantation of their companies' devices should not represent a major hurdle for adoption. The companies will have to demonstrate for specific indications, however, that the costs and risks of device implantation are outweighed by benefits such as reduced treatment burden and improved compliance.

The panelists agreed that companies will need to start thinking more about delivery methods at the earliest stages of development. Washer commented, "What we have found is that the physical way we deliver the vector makes a big difference in efficacy and outcomes." Danse argued that companies must begin to develop long-term delivery strategies earlier in the drug development process, following initial proof-of-concept, for competitive and defensive purposes. The panelists also agreed that reimbursement must be addressed early in the development process, including assessment of payer attitudes and education of clinicians and payers.

Pharma Panel: Lessons in Leadership - A CEO Perspective

David Guyer, MD, Partner with SV Life Sciences Advisers, led a panel discussion on issues faced by biotech CEOs. Topics included team building, interactions with the board of directors, professional backgrounds of biotech CEOs, and lessons learned from past mistakes.

Biotech CEOs come from a variety of professional backgrounds, including clinical medicine, scientific research and business management. **Samir Patel, MD, President and CEO of Ophthotech**, who began his career in academic medicine, said that many of the skill sets required of a physician carry over to corporate leadership. **"You have to make really tough, bold decisions at times that are based on evidence and based on weighing the risks and rewards. That's what you're used to doing."**

Dean Mitchell, President and CEO of Lux Biosciences and **Abbie Celinker, CEO of Eleven Biotherapeutics**, bring MBA and PhD credentials, respectively, to their CEO roles. They emphasized that building a senior leadership team with diverse experience and leading the team to a common goal are more important than the particular background of the CEO.

Regarding interactions between the CEO and board of directors, Mitchell stressed the importance of open and timely communications. "If it's a critical issue, if something is going off the rails, you actually turn up the dial and communicate even more." **David Redlick, a Partner with the law firm WilmerHale**, echoed the idea that communication should be open and transparent, particularly in times of crisis. **"If you go to someone with bad news, part of the discussion always comes around to 'When did you learn about this?' It's very important to say, 'Just a few moments ago.'"**

Dr. Guyer asked the panelists to think about mistakes they have made in the past and what they learned from those mistakes. Redlick, an attorney who has served on the boards of many life science companies, cautions CEOs involved with transactions to be forthcoming regarding past problems rather than allowing acquirers or underwriters to uncover such issues on their own. He also advises CEOs to be careful with their email communications. Abbie Celinker advises biotech CEOs to let the clinical data always drive important decisions, even if a change in strategy is required. She also advises new CEOs to avoid the temptation of letting the board override their own intuition on matters such as hiring, strategy and deals. **"If you are going to take the risks and have the rewards of being a CEO of a company, you really do have to trust your intuition and be willing to make mistakes and then fix them if you need to."**

Device Panel: Current Status and Future Promise of Premium IOLs

-John Barr, Executive Vice President and Global President, Bausch & Lomb Surgical
-Richard L. Lindstrom, M.D., Founder & Attending Surgeon, Minnesota Eye Consultants
-Seba Leoni, Vice President & Global Franchise Head, Cataract, Alcon
-Stephen Slade, M.D., FASC Surgeon, Slade & Baker Vision Center
-William J. Link, PhD, Managing Director, Versant Ventures
-Andy Corley,Yelroc Consulting

Andy Corley of Yelroc Consulting, who as Co-Founder and CEO of Eyeonics, Inc. pioneered the premium IOL channel, led a panel discussion regarding the status and future outlook for premium IOLs. **William J. Link, PhD, Managing Director of Versant Ventures**, shared data from Market Scope regarding current premium IOL penetration rates. This year, approximately 14% of the $3.5 million cataract procedures in the US will be performed using toric and presbyopia correcting IOLs (PC-IOLs). Link pointed out that this 14% penetration rate has resulted in a 38% increase in cataract surgical fees in the US and a 48% increase in IOL revenues for manufacturers.

Most of the panelists predicted that premium IOL usage in the US would be higher in 2013. Corley challenged this assumption suggesting that premium IOL units would be lower due to competition from laser cataract technology for premium purchases. **Stephen Slade, MD of Slade & Baker Vision Center**, said, “In our own practice, the number of presbyopia correcting IOLs that we have put in has dramatically risen, in both percentage and absolute numbers, in the 2 1/2 years that we’ve had femtosecond laser cataract surgery.” **Seba Leoni, Vice President and Global Franchise Head of Cataract at Alcon**, added, “We’re seeing a significantly positive effect in those accounts that currently have femtosecond lasers, relative to increases in premium procedures.”

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On the question of what will drive greater adoption of premium IOLs:

- **John Barr, Executive Vice President and Global President for Bausch & Lomb Surgical**, said that improved technology is needed for matching the right premium IOL to the right patient, based on what patients expect and what the lenses can deliver.

- **Richard Lindstrom MD** pointed out that premium cataract patients expect excellent refractive outcomes, but with current intra-operative technologies, **"We're not delivering on that promise. We need industry to help us with additional instrumentation to make it easier for us to generate refractive outcomes."**

- Slade believes that the introduction of the femtosecond laser to cataract surgery will drive greater overall penetration of the premium channel, because patients can easily relate to the benefits of a laser, but have a harder time understanding accommodating and multifocal IOLs.

- Corley noted that patients in the US would benefit from a greater choice of premium IOLs. In Europe, there are 44 different premium IOLs available, compared to just 3-4 in the US. The European market for premium IOLs has grown to match the size of the US market, despite the fact that most Europeans who choose premium IOLs have to pay 100% of the procedure cost, without any contribution from third party payers.

Seven years after the 2005 CMS ruling that created the premium cataract channel in the US, the current 14% market penetration of premium IOLs is well below the 25-30% that had been predicted years ago by Link, Lindstrom and others. The panelists remain optimistic, however, regarding the long-term prospects for the premium IOL market, still predicting that premium IOL penetration in the US will eventually reach 25-35%. Leoni pointed out that a large study conducted by Alcon found that 37% of patients would be willing to pay for premium cataract outcomes. Barr suggested that femtosecond laser technology has the potential to drive this number higher, based on its ability to deliver better outcomes. According to Link, premium IOL usage will continue to grow because benefits to patients, surgeons and the IOL companies are all aligned.

With improvements to the IOLs as well as the complementary technologies that will help deliver consistently better outcomes, Link suggested that premium IOLs could grow to half of the cataract market over the next decade.

Pharma Panel:
Developing an Ophthalmic Pipeline

Nicholas Galakatos, PhD, Co-Founder and Managing Director of Clarus Ventures, began the panel discussion with comments on productivity and innovation in R&D pipelines. R&D productivity in pharma and biotech, measured by the number of drugs developed per $1 billion of R&D spending (corrected for inflation), has steadily declined since 1950. **"In 1970, it took about $100 million to successfully develop a drug; in 2010, it took 10-times that."**

Scott M. Whitcup, MD of Allergan, Inc., said that some of the productivity issues within the industry have resulted from large pharmaceutical companies investing in huge, high-risk Phase 3 trials in pursuit of billion-dollar blockbusters. Allergan attempts to mitigate risk by building a balanced portfolio that includes lower risk programs and pursuing some opportunities that would be too small for big pharma.

Anthony P. Adamis, MD, Vice President and Global Head of Ophthalmology for Genentech, a member of the Roche Group, noted that Wall Street analysts are telling the large pharma companies that they must diversify their business models, because the returns on R&D expenditures are lower than the cost of capital. Instead, Genentech has "doubled down on innovative R&D," with greater selectivity regarding clinical programs and therapeutic areas, with an eye on future reimbursement. In order to prioritize Phase 3 programs, "We do very robust Phase 2 studies that are adequately powered to show statistical significance of the primary endpoint and the target product profile is defined well before phase 2 is completed."

Robert Y. Kim, MD, Vice President and Head of Pharmaceutical Product Development with Alcon, said that the company has built a successful model of targeted development of ophthalmic drugs based on known molecules. Following the acquisition by Novartis, Alcon now has access to more traditional drug development capabilities and to a broader range of therapeutics and delivery methods.

Paul Sieving, MD, PhD, Director of the National Eye Institute (NEI), National Institutes of Health (NIH), provided a government perspective on drug development. The NEI accounts for $700 million of the $30 billion annual NIH budget. "Our mission is not to be a drug discovery program, but rather to fund and to fuel the pipeline by making the basic discoveries that ultimately show up in company opportunities" that address the needs of the American people. "Our mission has to include partnering with industry at as many levels as we can."

Dennis Henner, PhD, Managing Director of Clarus Ventures, discussed the project prioritization and development process during his time as the head of research for Genentech. "At Genentech, we had a belief that if you invested in basic biological processes and coupled that with physician scientists who could work with the basic investigators and help direct them into clinical areas, that would ultimately pay off." Henner added, "At the same time, we had what I would call a controlled schizophrenic response," combining a focus on core areas of research with the belief that 20-30% of portfolio opportunities would emerge in unexpected ways out of core discovery areas. Lucentis is an example of such product; prior to its discovery, Genentech was not in the ophthalmology field.

The Impact of the Presidential Election on Innovation in the US and Beyond – Jim Mazzo

Bill Link introduced Jim Mazzo as "a leader in the industry for decades, who has played an important role, not only for the ophthalmic industry, but for the overall medical device industry," having served as the head of AdvaMed, the primary advocacy agency for the medical device industry.

Mazzo reviewed the impacts of the election outcome, which he characterized as "not a positive" for the ophthalmic and broader medical technology industries. Most immediately, if Congress is not able to come to a budget agreement, prescription drug and medical device user fee provisions could be subject to major challenges and changes. Over the next presidential term, the fact that at least one and up to three Supreme Court justices will be replaced "will have a huge impact on our industry," recalling the decision that the high court made earlier in 2012 on healthcare reform and the Affordable Care Act (ACA).

Mazzo discussed some reasons for concern within the medical device industry, including the movement overseas of American device makers, declining VC investment, the coming medical device excise tax, continued US and international regulatory delays and price controls in some countries. Although the President talks about the large number of new patients that will be insured under the ACA and the resulting positive impact on the US healthcare industry, Mazzo noted that 88% of these previously uninsured individuals will be under age 45 and will therefore not be significant consumers of ophthalmic products and services. Although there was hope that the 2.3% medical device excise tax might be aborted if the election outcome had been different, Mazzo now assumes that this tax will be implemented. Because of the potential dramatic impact on smaller companies, it is possible that the tax could be challenged for companies with less than $100 million in revenues.

As industry interacts with policy makers in Washington over the coming months, on issues such as the device tax, user fee legislation and repatriation of overseas profits, Mazzo suggests focusing on the basics: "The bottom line is that jobs and innovation do not know party lines."

Private Ophthalmic Device Companies

Highlights from Private Ophthalmic Device Company Showcase

A diverse group of thirteen private ophthalmic device companies presented their technologies and latest developments in brief eight-minute presentations. The broad range of products under development by these companies included novel diagnostics, ocular implants for presbyopia correction and late-stage retinal disease and devices for delivering drugs and therapeutic energy to the front and back of the eye.

Four companies presented diagnostic technologies that address applications such as retinal disease screening, continuous IOP monitoring for glaucoma patients and intraoperative wavefront aberrometry.

www.i-optics.com

i-Optics, based in the Netherlands, is a commercial stage company and leading pioneer in smart and superior eye diagnosis solutions. Their products are designed to be affordable, fast and easy to use by care providers all over the world to serve patients best and in the most convenient way.

What's new?

Cassini is a first-of-its-kind corneal topographer based on Color LED Topography. It enables superior diagnosis for fitting of standard and premium contact lenses, dry eye analysis, cataract and refractive surgery and corneal transplant. i-Optics launched the Cassini color LED topographer this past September at ESCRS, focused on corneal surface applications. Future generations, targeted at refractive surgery, corneal inlays and cataract surgery, are slated for 2013 and 2014. The company's EasyScan system enables early diagnosis of diabetic retinopathy, AMD and glaucoma. EyePrevent is a retinal-disease screening service for diabetic and other patients to help prevent blindness. The company raised a $10 million D-round earlier in 2012 to fund international expansion and product rollouts and plans to raise an additional $5 million by the end of the year. i-Optics hopes to achieve sales in excess of $10 million in 2013 and reach break-even by the end of the year. i-Optics is interested in establishing commercial partnerships for its Cassini and EasyScan systems.

www.maculogix.com

MacuLogix is a pioneer in the development of ophthalmic diagnostics for age-related macular degeneration (AMD) and is working with a number of leading pharmaceutical companies on the development of drugs for early AMD.

What's new?

The company is developing the AdaptDx™ diagnostic for AMD. AdaptDx™ measures dark adaptation and is the first practical diagnostic for AMD. It uses advances in measurement of dark adaptation to detect and track AMD from its beginning stages, similar to the routine use of perimetry for detection and tracking of glaucoma. The initial focus is on routine patient screening aimed at early detection and intervention. A product launch is planned for H2-2013. The company's second focus is the therapeutic market, in which the diagnostic would be sold along with AMD drugs and used as tool for tracking early disease progression. MacuLogix is already working with five drug companies using this approach.

The company has an initial 510(k) clearance for measuring dark adaptation and will apply for US clearance in early 2013 for use as an aid in diagnosing AMD. A CE Mark is planned for late 2013 or early 2014. MacuLogix has sold 17 prototype units and is planning a formal product launch in H2-2013. The company has raised $6 million in grants and venture capital. A Series B round is planned for 2013.

SENSIMED Triggerfish

www.sensimed.ch

Sensimed AG, a Swiss company, is directly positioned at the convergence of devices, treatment and information. Sensimed AG has been a commercial stage company for about two years, with a CE Mark and restricted commercialization in 20 countries through 15 distributors. With its principal focus on design, development and commercialization of integrated micro-systems for medical devices, Sensimed grows within a world-leading cluster for medical devices in the lake of Geneva area.

What's new?

Sensimed has developed a non-invasive soft contact lens-based solution, the SENSIMED Triggerfish®, that revolutionizes glaucoma management by providing continuous 24-hour intraocular pressure (IOP) profiles as well as modeling and analysis of IOP patterns. The 24-hour IOP profiles, centralized on a registry together with patient and treatment information, are processed by powerful modeling and learning algorithms. This process identifies pathological patterns used to differentiate indications and to personalize treatment to better target those pathological patterns. The company hopes to launch in 25 additional countries in 2013, including the US and China. A 510(k) has been filed in the US.

A reimbursement pathway is defined and the company hopes to receive a CPT Category III code by the end of 2012. Sensimed raised CHF 25 million (about $25 million) in Series A and B and is currently raising a Series C round of up to $25 million; a first closing of $17 million was recently completed and the company plans to raise an additional $8 million in a second closing.

WaveTec Vision™

www.wavetecvision.com and www.getorasystem.com

WaveTec Vision Systems, Inc. is a privately-held ophthalmic medical device company headquartered in Aliso Viejo, California. The company is focused on research, development, manufacturing and distribution of wavefront technology used during cataract surgery.

What's new?

After introducing its first aberrometer nearly three years ago, in December 2011 the company launched ORA™ (Optiwave™ Refractive Analysis), the fourth generation of its revolutionary system designed to take intraoperative wavefront aberrometry to a new level of precision. ORA is the first and only wavefront technology designed to help cataract surgeons provide better refractive outcomes for all cataract patients. The company's most recent clinical data demonstrates that the ORA System delivers more predictable refractive outcomes in cataract surgery, cutting the need for post-op refractive enhancements in half. The ORA System, particularly valuable in cataract patients that have had previous refractive surgery, reduces the need for post-op enhancement by 70-80% in these patients.

WaveTec has experienced consistent quarter-over-quarter growth over the past two years, in both procedures and system sales and expects over 12,000 procedures and over 30 system placements in Q4-2012. System utilization currently averages about 40 procedures per month. Over 55,000 cataract procedures have been performed to date; the annual run rate is 50,000 procedures and growing. This past April, WaveTec Vision raised an additional $16.5 million to commercialize its system.

Three companies presented competing corneal inlay technologies for the surgical correction of presbyopia.

AcuFocus™

www.AcuFocus.com and www.kamrainlay.com

AcuFocus Inc. is a privately held company located in Irvine, California. The company developed the KAMRA™ inlay for the treatment of near vision loss (presbyopia). AcuFocus is actively developing additional products. Some are adjuncts to the KAMRA inlay while others capitalize on the AcuFocus patent portfolio, small-aperture technology or manufacturing technology developed for the inlay.

What's new?

The KAMRA inlay is an intra-corneal inlay designed to create a small aperture effect, allowing the eye to see near and intermediate objects more clearly while maintaining distance vision. By applying the "depth-of-focus" principle commonly used in photography, the KAMRA inlay controls light transmission, allowing only central rays to reach the retina through a fixed 1.6mm aperture. AcuFocus has certified over 150 surgeons. The product is commercially available in 47 countries in Europe, Asia and the Americas. KAMRA received CE Mark approval in 2005 and in 2012 received approvals in Korea, Switzerland and Canada. In the US, the IDE clinical trial involving 507 patients is in progress. At 24-month follow-up, trial results show that KAMRA has exceeded FDA benchmarks on key endpoints involving visual acuity and refractive stability. 86% of patients said that they do not use reading glasses and 97% would have the procedure again. The KAMRA inlay has been implanted in over 16,000 patients worldwide including 11 ophthalmologists and three optometrists. The AcuFocus KAMRA inlay is a 2012 Medical Design Excellence Awards® Finalist.

Presbia®

The clear leader in near vision restoration™

www.presbia.com

Presbia is a leading ophthalmic device company focused on the development of the presbyopia-correcting Presbia Flexivue Microlens™, an innovative solution for the common age-related loss of the ability to read or focus on near objects.

What's new?

Presbia markets Flexivue Microlens, a presbyopia-correcting inlay outside the US. The product is a 3-mm lens, approximately 15 microns in edge thickness, implanted in the corneal stroma of the patient's non-dominant eye. The lens may stay in place permanently or can be easily removed and/or replaced if the patient's presbyopia advances and a stronger prescription is required. This procedure is a permanent yet reversible solution for presbyopia. In an international 64-patient post-market study of the Presbia Flexivue Microlens, at 12 months, 100% of patients achieved near visual acuity of 20/40 or better (versus only 2% of patients pre-operatively) and 71% achieved 20/25 or better. Patients typically lose about two lines of distance vision in their operated eye compared to the six lines of distance vision typically lost in monovision procedures. 20/20 binocular distance vision had been maintained in nearly all treated patients. Patient satisfaction rates in the study were very high. 97-98% of patients were happy with their uncorrected near and distance vision and 74% of patients were not using glasses for near vision.

RVO
REVISION OPTICS

www.revisionoptics.com

ReVision Optics, Inc., is a privately held corporation that is focused on the development and commercialization of minimally invasive implantable devices for the treatment of presbyopia.
The company's first product is the Raindrop™ Near Vision Inlay—a proprietary, patented solution for the improvement of near and intermediate vision by modifying corneal curvature.

What's new?

Until recently, the ReVision Optics (RVO) inlay was known outside the US as Vue+ and in the US as PresbyLens. Late this year,in preparation for a controlled commercial launch in Europe and Japan, the company harmonized the global brand under one name, Raindrop Near Vision Inlay. RVO believes that this name improves patient positioning and better reflects the technology. The product has the same 80% water content as the cornea. The Raindrop has received CE Mark and ReVision Optics is initiating a controlled launch in the European Union and Japan. The company is conducting a Phase III clinical trial under an IDE in the United States, with enrollment expected to be completed in the second half of 2013. Data from the US IDE trial, which is ongoing, shows that the Raindrop inlay improves near vision by about five lines and intermediate vision by about two lines, with minimal loss of distance vision.

In commercial and clinical sites, patient satisfaction rates have been 93-97%. The company will be initiating fundraising efforts in Q1-2013.

Two companies presented very different technologies that deliver energy to the back of the eye to treat retinal diseases.

2 Tech

www.2ctechcorp.com

2C Tech is a Colorado-based company that is developing a novel, breakthrough nanotechnology-based medical device, the SeeQ, to address unmet needs in degenerative retinal diseases such as AMD, diabetic retinopathy and retinitis pigmentosa.

What's new?

The SeeQ device improves the survival of degenerating retinal cells through cellular-level electrical stimulation and rescue. A single injection of SeeQ device constitutes billions of nanoparticles in a suspension. These nanoparticles produce electricity similar to a silicon solar cell, activated by normal ambient light entering the eye. No external power source is necessary. This electrical stimulation induces diseased retinal cells to generate protective growth factors. SeeQ stimulates the natural protective mechanism of the retinal cells and prevents disease progression. Periodic injections of SeeQ are required to stop the retinal degenerative process.

2C Tech has generated preclinical data demonstrating safety and efficacy of SeeQ based on anatomical, physiological and functional modalities. SeeQ-injected animals have shown significantly higher retinal cell survival rates and ERG/electrical activity versus controls and have outperformed control animals in a maze test. 2C Tech has an exclusive global license to intellectual property developed by the University of Colorado. Patent applications have been filed. 2C Tech is currently seeking Series A financing for completion of preclinical safety tests and Phase 1 human clinicals. Future funding rounds will address European clinicals in support of CE Mark and US Phase 3 clinicals in support of FDA approval.

ORAYA THERAPEUTICS

www.orayainc.com

Founded in 2007, Oraya Therapeutics, Inc. is a privately held company developing and commercializing a unique non-invasive therapy for the treatment and management of wet age-related macular degeneration (AMD). With headquarters in Newark, California, the company is actively supported by leading medical technology investors. Utilizing a low energy x-ray source, Oraya's IRay system is a stereotactic radiation delivery device designed specifically for treatment of wet AMD in an outpatient setting.
The treatment is intended as a one-time treatment to be used in conjunction with injected anti-VEGF agents, significantly reducing the frequency of those injections while maintaining or improving vision outcomes.

What's new?

At the first annual OIS in 2009, Oraya Therapeutics presented its plans for the INTREPID Study, a sham-controlled, double-masked study of the company's IRay system in conjunction with as-needed (PRN) anti-VEGF injections. The study enrolled 230 patients in five European countries at 21 sites. This challenging population had already been on anti-VEGF therapy for about 15 months. Study results were presented in September at the EURETINA meeting. Sham control patients required an average of 4.6 PRN anti-VEGF injections over 52 weeks, compared to only 2.0 injections for IRay treated patients. Visual acuity at 52 weeks was better in the IRay group by a mean of 6.8 ETDRS letters. With respect to safety, there were no cases of sight-threatening proliferative retinopathy and none are expected. Oraya has developed a commercial system which is currently under beta testing.

Two companies presented prosthetic implants that address patients with blindness or severe vision impairment due to end-stage retinal disease.

Second Sight

www.2-sight.eu

Second Sight Medical Products Inc., located in Sylmar, California, was founded in 1998 to create a retinal prosthesis to provide sight to patients blinded from outer retinal degenerations, such as retinitis pigmentosa. Through dedication and innovation, Second Sight's mission is to develop, manufacture and market implantable visual prosthetics to enable blind individuals to achieve greater independence. European Headquarters are in Lausanne, Switzerland.

What's new?

Second Sight's Argus II Retinal Prosthesis System is CE-marked in Europe. FDA approval in the United States is pending. Second Sight's initial indication for the Argus II System, covering severe to profound retinitis pigmentosa (RP), could address about 46,000 patients in Europe and the US. At an ASP of just under $100,000, which is reimbursed in Europe, the first indication alone represents a nearly $4.5 billion market opportunity. Second Sight is planning a second clinical trial in severe AMD, which represents a nearly $13 billion opportunity. EU revenues in 2012 will reach $2.3 million, in just four centers. In the US, following a unanimous panel recommendation in 2012, FDA approval is anticipated in Q1-2013 and commercial launch is planned for Q2. A US reimbursement pathway has been identified and a CPT Code is in place. Software upgrades under development for Argus II could provide enhanced acuity and future Argus III and IV systems could address significantly larger blind populations.

www.CentraSight.com and www.VisionCareInc.net

VisionCare Ophthalmic Technologies (VisionCare) is a privately held specialty medical device company engaged in the research, development, manufacture and marketing of proprietary implantable ophthalmic devices and technologies that are intended to significantly improve vision and quality of life for individuals with untreatable retinal disorders.

What's new?

VisionCare has developed the first FDA-approved telescope prosthesis demonstrated to improve vision and quality of life in individuals with end-stage AMD. The vast majority of these patients are in the Medicare population; the patients that VisionCare intends to serve with its device. The prosthesis is integral to the CentraSight® treatment program which has been created to help patients follow the necessary steps for proper diagnosis, surgical evaluation and postoperative care. The telescope implant technology is based on wide-angle micro-optics that, in combination with the optics of the cornea, create a telephoto system that magnifies objects in view.

While VisionCare's implantable telescope prosthesis is approved in the US and EU, the company's commercial focus is in the US. At OIS, the company announced that it had just received marketing approval in Canada. Medicare now provides reimbursement in most areas of the US. CMS has issued a HCPCS code for reimbursement for the device and the AMA has issued a CPT Code for surgeon reimbursement. Surgeon reimbursement is about twice the level of conventional cataract surgery.

One device company presented a novel product platform based on accelerated corneal cross-linking and another presented a drug delivery system designed to address multiple indications.

www.avedro.com

Avedro is a private company developing non-invasive ophthalmic devices, drugs and procedures based on accelerated cross-linking. Avedro's KXL™ System performs Lasik Xtra™ for restoring corneal biomechanical strength during Lasik and accelerated cross-linking for keratoconus and post-Lasik ectasia. More than 25,000 patients have been treated worldwide with the KXL System and Avedro's family of proprietary riboflavin formulations. Avedro is also developing the KXL II System with real-time eye tracking, dosimetry and programmable patterns for customizable correction of myopia and astigmatism using only cross-linking. The KXL System and Avedro's family of riboflavin formulations are CE Marked and commercially available outside the US.

What's new?

Avedro has completed its US Phase 3 studies for the orphan indications of keratoconus and post-LASIK ectasia. The clinical data demonstrates that the company's cross-linking system effectively stabilizes the cornea. There are 114 approved US clinical sites currently in three additional Phase 3 studies for more advanced technologies and four Phase 1/2 studies are planned for additional indications. The primary LASIK procedure, addressed by Avedro's Lasik Xtra, represents a much larger market opportunity, with 3.8 million annual LASIK procedures worldwide. Avedro is also developing the KXL II system, to correct low levels of myopia and astigmatism using precisely patterned cross-linking alone, without a laser or corneal incisions. In 2012, the first year of OUS commercialization, the company is on track for over 46,000 procedures.

www.eyegatepharma.com

EyeGate Pharma is a privately held, specialty pharmaceutical company dedicated to developing therapeutics for treating ocular disorders. Its proprietary, non-invasive EyeGate® II Delivery System (EGDS) is designed to achieve optimal therapeutic levels of drug in the anterior and posterior segments of the eye while simultaneously minimizing systemic distribution.

What's new?

The EGDS overcomes the shortcomings of current dosing approaches. Topical applications struggle with issues of insufficient ocular exposure, systemic exposure, high dosing frequency and compliance. Injections/implants present potential safety risks.
The company's first product, EGP-437, is the corticosteroid dexamethasone, re-formulated for delivery using EGDS. It has demonstrated that the EGDS doses substantially more drug more quickly than conventional methods, accelerating the onset of action and possibly reducing safety risks.

There have been more than 1,500 treatments performed in clinical studies with the EGDS. EGP-437 is currently in Phase 3 for anterior uveitis and in Phase 1 for scleritis. The Phase 3 uveitis study will enroll up to 200 subjects in over 40 US sites.
The top-line data is expected in March 2013. In clinical studies, the drug has been shown to work very quickly, leading to accelerated healing. In the Phase 2 uveitis study, a majority of patients had a complete response after just one treatment without a significant increase in IOP. EyeGate has also developed a method of delivering proteins to the back of the eye, which could ultimately result in an alternative delivery method for anti-VEGF agents for AMD.

-Stephen From, CEO, EyeGate

Highlights from Private Ophthalmic Pharma Company Showcase

Twelve private ophthalmic bio-pharma companies presented their technologies and latest developments in brief eight-minute presentations. The diverse group products under development by these companies included glaucoma treatments based on new mechanisms of action, sustained release delivery technologies and novel therapeutics for dry eye, wet and dry AMD and other ophthalmic indications.

Three companies presented development stage glaucoma therapeutics that address IOP lowering through increased outflow through the trabecular meshwork, which represents a new mechanism of action.

aerie
pharmaceuticals, inc.

www.aeriepharma.com

Aerie Pharmaceuticals is a privately held, clinical-stage biotechnology company dedicated to the discovery and development of novel treatments for glaucoma. All technology of the company is based on internal discovery R&D and is protected by a strong IP portfolio. The US-based company is located in Bridgewater, NJ and in Research Triangle Park, NC. Investors in Aerie are TPG Biotech, Alta Partners, Clarus Ventures, Sofinnova Ventures and Osage University Partners.
In February 2011, the company closed a Series B financing of $30 million.

What's new?

Aerie Pharmaceuticals' pipeline includes three new options for the treatment of glaucoma. The lead product, AR-12286, is a selective Rho-kinase (ROCK) inhibitor that that would be the first agent to lower IOP by increasing trabecular meshwork outflow. A Phase 2/3 study is ongoing and two Phase 3 studies are planned. Aerie is also investigating PG286, a fixed combination of AR-12286 and travoprost which is being advanced to Phase 2b. PG286 increases outflow via both uveoscleral and trabecular meshwork pathways. If approved, it would be the first prostaglandin fixed-dose combination in the US. Both AR-12286 and PG286, dosed once daily, could compete as second-line glaucoma treatments. Aerie's third compound in Phase 2 clinical development, AR-13324, is a novel dual action glaucoma drug that would be the first to address both inflow and outflow, with the potential to become first-line, once-daily therapy.

amakem THERAPEUTICS

www.amakem.com

Amakem, headquartered in Belgium, is a kinase platform company focusing on ophthalmology and developing new treatments for serious eye conditions. Amakem's product pipeline is based on its unique 'Localized Drug Action' platform which generates novel kinase inhibitors that minimize systemic exposure with the aim of reducing side effects. Incorporated in January 2010, Amakem has raised approximately €21 million.

What's new?

The company's lead candidate, AMA0076, is a novel, highly potent Rho kinase inhibitor targeted at the treatment of glaucoma. AMA0076 is designed to effectively lower IOP while avoiding the side effects typically associated with this drug class; unacceptable hyperemia, or redness, which limits dosing and therefore efficacy. Based on Amakem's "Localized Drug Action" platform, any drug that remains outside the eye is metabolized and inactivated before it can cause hyperemia. In preclinical models, AMA00076 delivered better efficacy than other available ROCK inhibitors with no significant hyperemia. An ascending dose Phase 2a trial began in September and is ongoing, with final results expected in 2013. Amakem has also demonstrated proof-of-concept for the technology in COPD and asthma.

INOTEK PHARMACEUTICALS

www.inotekcorp.com

Inotek, located in Lexington, MA, is a leader in the development of innovative drug candidates to address significant diseases of the eye, with a major focus on glaucoma. The Company is also advancing a broad pipeline of PARP inhibitors and SOD mimetics that alleviate oxidative injury and inflammation, which it believes may address significant unmet medical needs in retinal diseases, such as the dry form of age-related macular degeneration (dry AMD).

What's new?

Inotek is in late stage Phase 2 development of trabodenoson (formerly INO-8875), a potential first-in-class topical highly selective Al receptor subtype adenosine-mimetic. It is a novel glaucoma treatment that works by increasing outflow through the trabecular meshwork. Clinical data has shown IOP reduction of about 7mm Hg at 28 days, which is in-line with prostaglandins (PGs) and superior to current second-line treatments. Ocular tolerability has been very good. Although Inotek has only tested twice-daily (BID) dosing to date, there is a potential for once-daily (QD) dosing. If QD dosing can be achieved while delivering superior efficacy to PGs, or similar efficacy with improved safety and tolerability, trabodenoson could be positioned as first-choice monotherapy. Inotek is planning two additional Phase 2 studies, one that adds trabodenoson therapy to PG users that need additional IOP lowering and one that involves dose escalation with both BID and QD dosing over 60 days.

Two companies presented very different approaches to sustained release drug delivery.

www.avalanchebiotech.com

Founded in 2006, Avalanche Biotechnologies is a privately held company that develops technologies and products for sustained delivery of therapeutic proteins to the eye for treatment of wet age-related macular degeneration (AMD) as well as other ophthalmologic disorders such as diabetic retinopathy, retinal degeneration and glaucoma. Founded by a team of serial entrepreneurs, including Prof. Mark S. Blumenkranz, Chairman of Ophthalmology at Stanford University and Prof. Steven D. Schwartz, Chief of Retina at UCLA Jules Stein Eye Institute, the company is located in San Francisco, CA.

What's new?

Avalanche Biotechnologies' lead product, AVA-101, is currently in Phase 2 for wet AMD. The product addresses the need for sustained delivery of anti-VEGF proteins, in order to reduce the treatment burden and provide long-term, sustained therapeutic levels. The goal is the effective long-term treatment of wet AMD without the need for frequent intraocular injections. The company's technology delivers an anti-VEGF payload inside a nanotechnology particle called AAV, which creates an "Ocular Biofactory™" that secretes therapeutic protein over a period of years. AVA-101 is injected subretinally in a 20-minute pars plana vitrectomy procedure under local anesthesia. AVA-101 is currently in clinical trials for the treatment of neovascular AMD. A small Phase 1 study conducted in 2012 met its primary safety endpoint and early signs of a therapeutic effect are emerging, as AVA-101 showed a marked reduction in the need for anti-VEGF re-treatments during the ten month trial period.

www.ocutx.com

Ocular Therapeutix, Inc. is a privately held company based in Bedford, MA, focused on the development and commercialization of ophthalmic therapeutic products using its proprietary polyethylene glycol hydrogel technology.

What's new?

Ocular Therapeutix recently completed a Phase III premarket approval (PMA) study for its ocular hydrogel sealant (ReSure® Sealant), is currently undergoing clinical trials for drug-eluting punctal plugs for treatment glaucoma and post-operative inflammation and is researching therapeutic agents for back-of-the-eye diseases. Ocular Therapeutix's first product, the ReSure® Adherent Ocular Bandage, is CE Mark approved and commercially available in select international markets. In the US, the PMA filing for ReSure Sealant should be completed by the end of 2012, with possible FDA approval in 2013.

Ocular Therapeutix is developing drug-eluting hydrogel punctum plugs that provide steady release over two to three months. The first application involves sustained release travoprost for glaucoma. A recently completed Phase 2 pilot study demonstrated stable IOP reduction of about 7 mmHg, typical for prostaglandin drops, over a two month period using a single plug, with no increase in hyperemia (redness). The company plans to study a three month duration travoprost plug in early 2013, with possible initiation of Phase 3 in late 2013. A sustained release dexamethasone punctal plug for post-surgical inflammation is entering Phase 2 and could progress to Phase 3 in 2013. Ocular Therapeutix is collaborating with pharmaceutical partners on an injectable hydrogel slurry with anti-VEGF agents for retinal diseases.

Two companies presented new treatments under development for the challenging indication of dry eye disease.

ELEVEN BIOTHERAPEUTICS

www.elevenbio.com

Eleven Biotherapeutics' AMP-Rx platform allows for the discovery and development of biotherapeutics that can be optimized for ophthalmic applications, an area where protein innovation was previously less typical. By attenuating underlying inflammatory mechanisms, Eleven's AMP-Rx technology and expertise can play a significant role in discovery and developing novel biotherapeutics to treat a number of ophthalmic diseases such as ocular surface diseases (dry eye, allergy, etc.), neurodegeneration associated for example with glaucoma, and dry AMD, uveitis and retinal vasculopathy such as wet AMD and diabetic macular edema. Eleven has developed a suite of pipeline candidates to address ophthalmic disease.

What's new?

Eleven Biotherapeutics' lead program is EBI-005, a topical IL-1 antagonist that is now in Phase 1 clinical development. EBI-005 is a differentiated protein that treats dry eye disease by blocking IL-1, a master regulator of inflammation that drives many ocular diseases. With EBI-005, the company was able to move from design to development in less than nine months using its simultaneous approach to drug discovery rather than the traditional serial approach. EBI-005 is currently in Phase 1 for dry eye disease. The company's clinical strategy calls for Phase 2b for this indication in 2013 and Phase 2b for severe ocular allergy in 2014. In addition, Eleven Biotherapeutics has a broad pipeline of tuned cytokine inhibitors to treat other ocular diseases.

-Abbie Celniker, CEO, Eleven Biotherapeutics

www.sarcode.com

SARcode Bioscience, Inc. is a privately held venture backed biopharmaceutical company founded in 2006 and located in Brisbane, CA with the initial objective to develop a novel LFA-1 antagonist for topical treatment of ocular inflammatory disease. SARcode Bioscience is developing novel molecules that specifically target chronic T-cell mediated inflammation in ophthalmic disease. SARcode has exclusive worldwide development and commercial rights to the LFA-1 program. The SARcode development platform is built upon a novel class of integrin inhibitors that targets T-cell mediated chronic inflammation. In December 2006, SARcode secured $25 million in financing co-led by Alta Partners and Clarus Ventures. Series B investors included Rho Ventures and Sofinnova Ventures.

What's new?

SARcode Bioscience is in Phase 3 development of lifitegrast, a novel LFA-1 antagonist for topical treatment of dry eye. In the recently completed 588-patient OPUS-1 Phase 3 study of lifitegrast for dry eye disease, lifitegrast demonstrated statistically robust superiority over placebo in the improvement of inferior and total corneal staining scores from baseline to week 12. Lifitegrast also significantly improved the most commonly reported symptoms of dry eye disease in the study, which were ocular discomfort and eye dryness. Lifitegrast was well tolerated and there were no unexpected or serious ocular adverse events. SARcode is currently initiating a long-term safety study (SONATA), as well as a second pivotal Phase 3 confirmatory study (OPUS-2). The company is targeting an NDA submission in 2014 and FDA approval in the first half of 2015.

-Charles Semba, CMO, SARCode Bioscience

Two companies presented therapeutic products that address AMD with new mechanisms of action, including a treatment in Phase 3 development to address dry AMD, for which there are no approved treatment options.

www.macuclear.com

MacuCLEAR Inc.™ is a specialty clinical-stage pharmaceutical company focused on discovering and developing novel solutions for vascular disorders of the eye – specifically dry AMD. Dry AMD represents a huge unmet need, with a market potential of greater than $20 billion. The company has six issued patents, IND and Fast Track Status and has completed its groundbreaking Phase 1/POC human trial.

What's new?

MacuCLEAR is in Phase 3 development of MC-1101, invented by Dr. George Chiou who pioneered Timolol for glaucoma. MC-1101 is a novel preservative-free eye-drop treatment, a small molecule vasodilator that has been used previously as an anti-hypertensive. This known safety profile reduces regulatory risk. The company's approach to treating dry AMD is based on addressing vascular insufficiency as a root cause of the disease, a challenge to the conventional wisdom regarding the pathogenesis of AMD.
The company is currently conducting a 60-patient Phase 3 trial. A key finding of the study thus far is the successful migration of the drug to the back of the eye which increased choroidal blood flow in the back of the retina. After initial results of the Phase 3 trial are reported in late 2013, the trial could be expanded to include an additional 440 patients. MacuCLEAR has executed its strategic plan so far on less than $6 million. MacuClear will need to raise an additional $10-15 million to fund the expanded Phase 3 study. The company has 12 additional compounds in its pipeline targeting diabetic retinal diseases, glaucoma and Stargardt's Disease.

www.ophthotech.com

Ophthotech Corporation is a privately held biopharmaceutical company based in Princeton, NJ focused on developing and commercializing therapies for dry and wet AMD. Ophthotech is developing a pipeline of compounds with strong scientific foundations for the treatment of AMD, with the goal of bringing them to market in an accelerated manner. Ophthotech's venture investors include SV Life Sciences Advisers, Novo Ventures, HBM Partners and Clarus Ventures.

What's new?

Ophthotech's lead compound, Fovista™, a PDGF-B inhibitor, recently demonstrated superior efficacy over Lucentis® monotherapy in a large, controlled wet AMD trial. In this Phase 2b clinical trial of 449 patients with wet AMD, Fovista™ (1.5 mg), administered in combination with Lucentis® anti-VEGF therapy, resulted in a 62% increase in mean vision compared to Lucentis® monotherapy. Ophthotech plans to initiate Phase 3 development of Fovista in H1-2013. Despite the fact that this market is on track to approach $5 billion in global sales in 2012, anti-VEGF monotherapy has important limitations. A majority of patients do not achieve significant visual gain or reach final visual acuity of 20/40 and 25-30% of patients lose vision. Ophthotech believes that its anti-PDGF approach complements the effects of anti-VEGF therapy by attacking the underlying biology of wet AMD.

Ophthotech's C5 inhibitor (ARC 1905), in development for wet and dry AMD, has demonstrated positive data in a single arm Phase 2a study. ARC 1905 has been studied in 47 patients with geographic atrophy. Data from this trial will be available for presentation in Q1-2013.

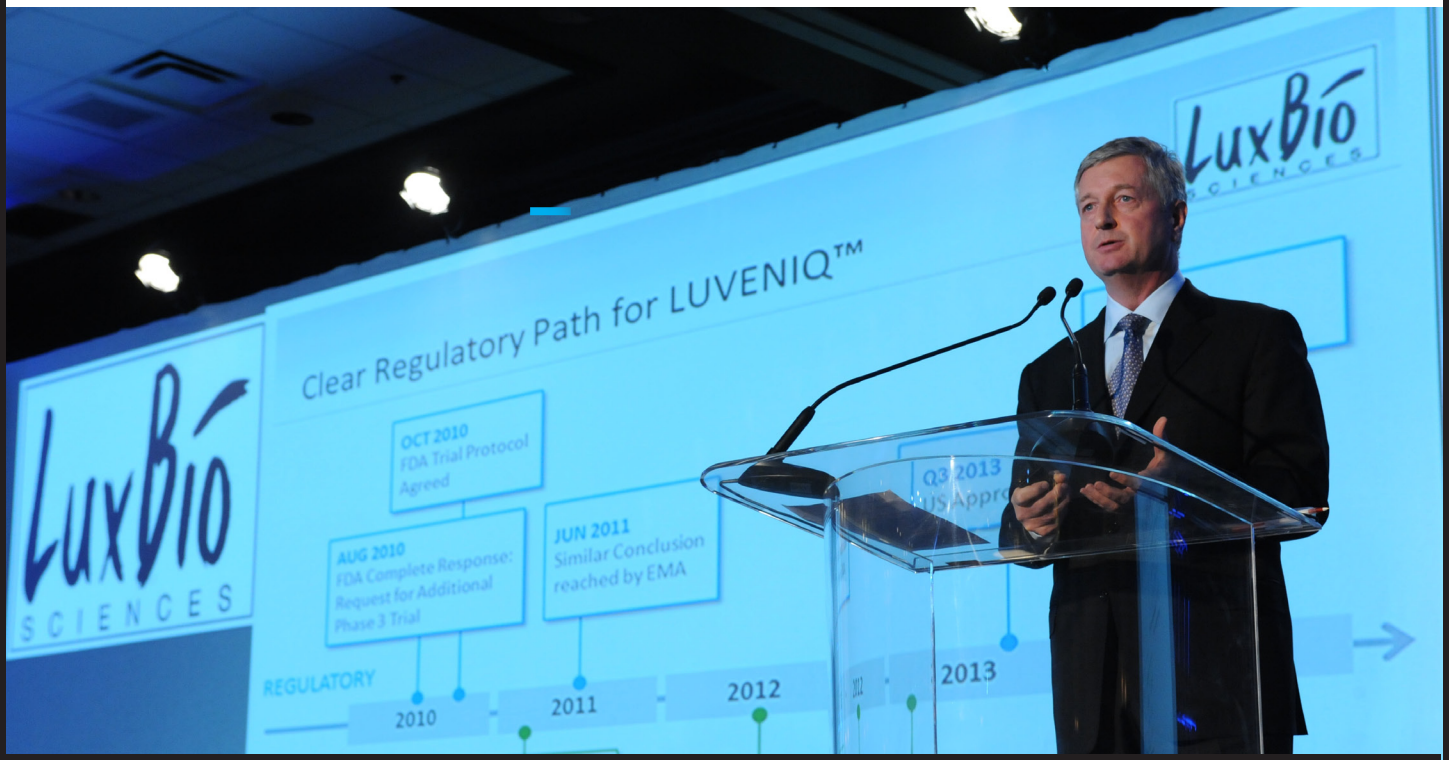
Three additional companies presented pharmaceutical technologies that address other unmet needs in ophthalmology.

www.luxbio.com

Lux Biosciences is a clinical stage biotechnology company specializing in the development and commercialization of innovative medications for serious ophthalmic diseases. With a Phase 3 clinical trial almost complete and several exciting earlier-stage projects, Lux Biosciences is building a revenue-generating, high-growth and sustainable ophthalmic company. Lux Biosciences is planning to submit an NDA and MAA to the FDA and EMA, respectively, for Luveniq in noninfectious uveitis, affecting the intermediate or posterior segments of the eye, in early 2013. Luveniq has orphan designations in both the US and EU.

What's new?

Lux Biosciences' lead product, Luveniq, is in Phase 3 development. Luveniq is targeted as an alternative to steroids for the 250,000 patients in the US and Europe with intermediate or posterior uveitis. After an August 2010 request by the FDA for an additional Phase 3 trial, the company began enrollment of a new 155-patient study in February 2011 and recruited the last patient in June 2012. Top-line data will be available in January 2013. Management believes that there is a high probability of a positive trial outcome. After a priority review, Lux Biosciences anticipates FDA approval in Q3-2013 and EU approval in mid-2014. Internal market research with ophthalmologists demonstrated 80% rating the product profile as excellent and 80% saying that they would use Luveniq to spare the use of steroids. The company believes that Luveniq represents a peak US/EU revenue opportunity of over $650 million.



-Dean Mitchell, CEO, Lux Biosciences

www.mobiustherapeutics.com

Mobius Therapeutics, founded in 2006, is a commercial stage venture focused on ophthalmic surgery solutions. Mobius is housed within the Center for Emerging Technologies in St. Louis, Missouri. Mobius represents a new model in ophthalmic ventures. Mobius addresses a $400-$475 million opportunity with capitalization fractional versus traditional ventures.

What's new?

In February 2012, Mobius Therapeutics gained FDA approval for an on-label version of mitomycin-C which has been used off-label in ophthalmology for decades to modulate wound healing. Mobius has partnered with the FDA in a six year long process to bring on-label ophthalmic mitomycin-C, an antimetabolite used to modulate wound healing and prevent scarring following ocular surgery. Mitosol® was launched in July 2012 for its first approved indication, glaucoma filtering surgery. The product addresses problems associated with sourcing from compounding pharmacies, sterility, transfer and disposal, toxicity, shelf life, waste and dosing irregularities. Mitosol® provides a single dose, within a closed fluid system assuring OR safety; sterile transfer is AORN compliant. Storage is at room temperature for up to 24 months vs. the current standard of 2 weeks, refrigerated. Potency and formulation are consistent; surgical technique is unchanged. Mitosol® is covered by two issued patents, four pending patents and three orphan drug designations. At OIS, Mobius announced that a new HCPCS J-code will become effective in January 2013. Supplemental NDAs are in process for two additional Mitosol indications: laser vision correction using surface ablation and pterygium surgery. Together with glaucoma surgery, these indications represent over 1.2 million annual procedures globally.

www.thrombogenics.com

ThromboGenics is a biopharmaceutical company focused on developing and commercializing innovative ophthalmic medicines. ThromboGenics is listed on the NYSE Euronext exchange under the symbol THR and is headquartered in Leuven, Belgium, with offices in Iselin, NJ (US) and Dublin, Ireland.

What's new?

ThromboGenics received FDA approval in October 2012 for its lead product JETREA® (ocriplasmin) for the treatment of symptomatic vitreomacular adhesion (VMA), sometimes referred to as Vitreomacular Traction (VMT) and will soon launch in the US. JETREA Phase III results were published in NEJM in August and FDA approval came in October. A CHMP opinion is expected in Europe in January 2013, followed by anticipated EU approval in March 2013. In March 2012, ThromboGenics signed a strategic partnership with Alcon (Novartis) for the commercialization of JETREA outside the US. If approved in Europe, Alcon could launch JETREA there in 2013. Under the Alcon agreement, ThromboGenics could receive up to €375 million in up-front and milestone payments, plus significant royalties. The company's market research suggests that there are about 500,000 eligible patients in the US and Europe. The US sales and reimbursement team has been hired and is preparing for the January launch. ThromboGenics has focused on its reimbursement and market access strategy and does not expect any reimbursement issues following US launch. ThromboGenics and Alcon intend to co-develop JETREA® for a number of new vitreoretinal indications. ThromboGenics is also exploring anti-PlGF (Placental Growth Factor) for the treatment of ophthalmic indications.

Highlights from Private Ophthalmology IT Company Showcase

Michelle Snyder, Executive-in-Residence with InterWest Partners, introduced the IT Company Showcase with an overview of the intersection of information technology, the consumer and healthcare. Snyder described the factors that are contributing to a "perfect storm" in digital health today, including rising healthcare costs, declining health of the population, increasing consumer decision-making, and responsibility for payment and the proliferation of mobile technology and social media. Digital health funding has more than doubled over the past three years, to $1.4 billion in 2012, supporting 2,100 digital health companies currently in operation. Some of the trends that are shaping the current wave of companies include:

- Aging in Place - Home sensors/monitors and connectivity with caregivers, to address people's desire to stay in their homes as they age
- Consumer Wellness/Tracking - Wearable sensors to track activity, eating, sleep, etc.; an estimated $1.5 billion market in 2013
- Information Transparency - Providing cost and quality information to consumers as they become increasingly responsible for healthcare decisions and payment
- Health Listening - Aggregating health-related posts from social media sites and packaging this information for medical product companies and healthcare providers

Four private IT companies presented technologies and business models that build on some of the trends outlined in Snyder's presentation.

ASSORT®

www.assort.com

ASSORT is a privately held ophthalmic software developer, based in Australia, that has been active in the cataract and refractive surgery field for 20 years.

The ASSORT software products are unique and have extensive international patent and trademark protection. These innovative software products fill the need in the ophthalmic industry for a computerized surgical management system that complements electronic medical records, office management and billing systems. These clinically useful software products offer increased sophistication to computer-driven femtosecond laser cataract and LASIK surgeries.

The flagship ASSORT® program provides confidential in-house analysis, tracking and reporting of cataract, refractive and glaucoma surgery outcomes, with the goal of fine-tuning surgical parameters to improve visual outcomes. A web-based application assists with planning and troubleshooting for toric IOLs and femtosecond laser LRI incisions. The iASSORT program performs astigmatic analyses using the topography and/or wavefront values provided by the diagnostic instrument into which the software has been installed; the software is interfaced with more than 10 topographers from leading manufacturers. The VECTrAK program provides a comprehensive set of astigmatic vector analysis tools based on the Alpins Method. At OIS, ASSORT was seeking equity-based partners and partnerships for international marketing and distribution.

DigiSight™ Technologies, Inc

www.digisight.net

Founded in 2009 by leading ophthalmology innovators Dr. Mark Blumenkranz and Dr. Daniel Palanker of Stanford University, DigiSight Technologies™, Inc. develops clinically impactful ophthalmology interventions that are delivered through mobile devices (e.g., iPhone, iPad) and which seamlessly connect patients and physicians. DigiSight provides cloud-based storage and home monitoring. The company's mission is to serve as the dominant universal platform to facilitate enhanced vision testing, rich data exchange and communication between patients and physicians and by extension as a bridge to industry and payers.

Their SightBook™ app, which will be released commercially at this year's AAO joint meeting, enables patients to monitor their vision while away from the doctor's office and transmits test data securely and in real time to their designated physicians, enabling doctors to deliver personalized treatment for chronic disease efficiently and effectively.

As a first target, DigiSight has identified intravitreal injections for AMD and the need to optimize treatment through reproducible home vision measurement and personalization of dosing - to detect disease progression and bring patients in for treatment precisely when needed. The system architecture consists of secure Internet data storage, patient self-testing on smart phones or tablets using the SightBook™ app and connection to ophthalmology practices. Clinical studies would also benefit from the additional data that could be gathered and reduced frequency and cost of study visits, using home monitoring.

doximity

www.doximity.com

Doximity is the first "real-name" authenticated online professional network designed exclusively for US physicians, supporting them in delivering faster, smarter treatment and managing their own practice. The largest and fastest growing online network for physicians, with 105,000 physician members to date, membership is projected to reach approximately 140,000 by the end of 2012, representing 20% of US physicians. Three of the top five medical schools (Stanford, UCSF and Penn) have partnered with Doximity to run their alumni networks. More than 2 million physician-to-physician connections have been made on the Doximity network. US physicians conduct roughly 1,000 referral/expert searches on Doximity every day.

One-third of physicians share a private phone number in their profiles to facilitate communication with referral colleagues. The average physician member now has 22 colleagues on the network which now has a total of 2.5 million connections between members and supports over 10,000 secure messages each day. Among US ophthalmologists, 15% are currently Doximity members.

A key benefit is improved connectivity between primary care physicians and the specialists to whom they refer patients. Physicians can use their iPhone, Android device, or desktop computer to quickly and securely connect with nearly any US physician to collaborate on patient care or find the right medical expert for a patient. Doximity recently secured $17 million Series B financing led by Morgenthaler Ventures.

ZocDoc
Get well sooner.

www.zocdoc.com

ZocDoc addresses the issue of patient access to physicians across the US. The service provides an online tool for patients to find and schedule appointments with doctors and other medical specialists in 31 major US metropolitan markets and more than 1,500 cities.

With the service, patients avoid the hassle of waiting on hold, searching for a good doctor, or wondering whether a doctor takes a particular insurance. The average wait time to schedule a physician appointment in the US is about three weeks. 91% of patients find this unacceptable and 45% delay seeking medical care because of the arduous scheduling process. ZocDoc member patients can schedule appointments within three days and can easily find doctors who take their insurance.

Participating doctors and dentists benefit by attracting new patients and alleviating the productivity lost from last minute cancellations by filling those available appointments with ZocDoc patients. Optometrists and ophthalmologists obtained an average of six new appointments per month per doctor in October 2012 via ZocDoc. The company's patient base also represents a favorable payer mix, with 83% PPO members and another 7% cash pay.

In June 2012, the company introduced ZocDoc en Español, making it easier for Spanish-speaking patients to use the service. This past October, ZocDoc introduced ZocDoc Check-In, allowing ZocDoc's 1.9 million monthly users to be able to fill out medical forms online in advance of their visit.

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"I only attend events that provide the most comprehensive education in the most efficient manner. OIS is that meeting. The intersection of clinical, financial and company perspectives in a one day forum enables myself and our team to stay current and add value to our business partners in the ophthalmology space".

–Evan M Norton, Director, Abbott Ventures

"Presenting RVO's technology at OIS has attracted a lot of interest from investors, clinicians, and strategic companies. Everyone leaves OIS with a better vision of the future of the ophthalmic industry".

–Randy Alexander, Chairman, ReVision Optics

"OIS gives industry a forum to interact in a meaningful way with clinicians and private companies which results in excellent synergy. I came away with a deeper understanding of how industry can help".

–Joseph Markoff, MD, PhD, Global Director for Scientific Affairs in Ophthalmology, Merck Inc.

www.oisascrs.com