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Hawaiian Eye and Retina 2006: More Good News for AMD Patients and Presbyopes

Last week in Maui, Slack, Inc. hosted its annual Hawaiian Eye 2006 and Retina 2006 educational programs. Forecasts for rain proved to be unreliable, which was good news for the record number of attendees: over 800 ophthalmologists and about 1,200 total participants.

Highlights of the Retina 2006 program:

(1) presentation of additional outrageous Phase III data for Genentech's Lucentis for wet AMD, (2) growing off-label use of intravitreal Avastin for a number of retinal indications, and (3) diminishing interest in Macugen, Visudyne/PDT, and intravitreal triamcinolone. There was no new information to drive changes in opinion regarding Alcon's Retaane, which is about

to complete enrollment in its risk-reduction trial but will require 4-year follow-up, and OccuLogix' RHEO Procedure, for which pivotal trial data will be published in the coming weeks.

ANCHORs Aweigh, DNA – Lucentis Raises the Bar, Again

On January 14 at Macula 2006 in New York, and again on January 17 at Retina 2006 in Hawaii, one-year data from Genentech's pivotal ANCHOR study was reported. Unlike the shamcontrolled MARINA study, the results of which were previously reported, ANCHOR is a head-to-head study

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Visual Quality and Presby-IOLs Dominate Cataract/Refractive Track at Hawaiian Eye

The cataract and refractive track at Hawaiian Eye 2006 focused on:

- New technologies that are taking post-surgical quality of vision to new levels, including aspheric IOLs, wavefront-guided laser vision correction with advanced methods of registration, and femtosecond lasers
- The rapid adoption of the first generation of surgical products for presbyopia, and growing anticipation regarding technologies under development
- How these technologies are blurring the lines between cataract and refractive surgery, and providing an opportunity for surgeons to establish longer-term patient relationships.

Accommodating Lenses: Increasingly Seen as the Ideal IOL Solution for Presbyopia

The surgical presbyopia revolution is being driven by two multifocal IOLs (Alcon's ReSTOR and AMO's ReZoom) and one accommodating IOL (eyeonics' crystalens), supported by last year's CMS ruling that has facilitated payment for and adoption of these new products. It is impossible at this point to declare any of these the "best" product; it is becoming clear that each of them has its own advantages and drawbacks, patients that are good candidates and those that are not, and surgeon supporters and detractors.

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comparing intravitreal Lucentis to a treated control using Visudyne photodynamic therapy (PDT) in patients with neovascular (wet) age-related macular degeneration (AMD). The study enrolled patients with predominantly classic lesions, for which Visudyne has already shown benefit over a sham control and been granted FDA approval.

As such, this was supposed to be a much more challenging trial for Lucentis. And the Patriots and Colts were supposed to be playing for the AFC championship this weekend.

The results of ANCHOR were very consistent with the previously reported results of MARINA, despite differences between the trials with respect to lesion **type and control arm.** The results appear to support the superiority of pan-VEGF blockade over the singleisoform approach employed by Macugen: Lucentis has a strong anti-permeability effect in the first several days, reduces retinal thickness as early as day one, and leads to significant visual improvement by day 14. The ANCHOR study included 423 patients, randomized 1:1:1 to monthly injections of 0.3mg and 0.5mg of Lucentis and to the Visudyne/PDT control arm. Of 83 centers, 71 were in the US. Over 95% of lesions were predominantly classic. Compliance was good: 89% for the PDT control group, and 91% and 94% for the 0.3mg and 0.5mg Lucentis groups, respectively. Top-line one-year results of the study are summarized in Table 1.

The safety profile of Lucentis continues to appear favorable as well, with serious ocular adverse events such as endophthalmitis and inflammation each occurring in less than 1% of patients. Non-ocular serious adverse events were also infrequent and well-balanced, except for certain cardiovascular events such as myocardial infarction, which occurred with slightly higher frequency in the 0.5mg treatment arm than in the other two arms (2.1% versus 0.7%). However, the overall numbers are small and differences are not statistically significant. It is also worth noting that the Lucentis pivotal trial enrollment involved fewer cardiovascular exclusions than did the Macugen studies.

Genentech has not announced whether is has chosen to file for approval for the 0.3mg or 0.5mg dose of Lucentis. However, comments from company management suggest a bias toward the 0.3mg dose, which would be the more conservative choice and one with "low

likelihood of being wrong." While efficacy was marginally better with the higher 0.5mg dose, the lower dose would avoid many of the safety questions that might be raised by the FDA and by adopting retina specialists. Genentech has not yet been notified that the FDA will grant an expedited review, but we view this as highly likely.

Monthly dosing of Lucentis will not likely remain the long-term approach. Two ongoing Phase IIIb studies are

	Lucentis (0.3 mg dose)	Lucentis (0.5 mg dose)	Visudyne/PDT Control
Primary Endpoint: Maintaining Vision: Loss of <3 Lines of VA	94.3%	96.4%	64.3%
Secondary Endpoints:			
Vision Improvement: Gain of 3+ Lines	35.7%	40.3%	5.6%
Vision Improvement: VA of 20/40 or better (pre-op → post-op)	1.4% → 31.4%	4.3% → 38.6%	0% → 2.8%
Extreme Vision Improvement: Gain of 6+ Lines	6.4%	12.2%	0%
Severe Vision Loss: Loss of 6+ Lines	0%	0%	13.3%
Mean Gain or Loss in Letters of VA	+8.5	+11.3	-9.5
Mean Difference vs. Control: Gain or Loss in Letters of VA	+18.0	+20.8	

Table 1. Phase III ANCHOR Study Results: Percentages of patients at one year achieving specified visual acuity (VA) outcomes, as measured by the ETDRS eye chart.

investigating less frequent dosing regimens, and provide a glimpse into the future of Lucentis dosing. In the PIER study, Lucentis is administered monthly for the first three months and quarterly thereafter. In the SAILOR study, Lucentis is administered monthly for three months and asneeded thereafter based on re-treatment criteria. Regular follow-up exams using OCT imaging should provide physicians with the data needed to determine when the latest dose of Lucentis is "wearing off." Genentech is waiting until these dosing strategies are sorted out before it pursues a longer-acting or sustained-release formulation.

A new definition of AMD treatment success. At Hawaiian Eye, Quinton C. Oswald, Genentech's Vice President of Sales and Marketing, Tissue Growth and Repair, commented that the company remains committed to helping the 60% or more of patients that don't respond to Lucentis. Incorporated within this comment is a shift in the way success will be defined for wet AMD treatments, from a paradigm of <3 line vision loss to one of \ge 3 line vision improvement. According to this new definition of effectiveness, nearly 95% of Visudyne and Macugen patients are non-responders.



Off-Label Use of Intravitreal Avastin Gains Momentum

The off-label use of intravitreal Avastin dates back to last summer, when Philip Rosenfeld, MD of the Bascom Palmer Eye Institute in Miami presented his initial positive experience at the ASRS in Montreal. Since that time, it has been picked up by the "early adopters" within the retinal community. It is estimated that over 5,000 intravitreal Avastin injections have been administered in the US. At Retina 2006, at least three lecturers stated that their institutions had administered 500 or more injections, and there was mention of a safety registry that has logged nearly 4,000 cases.

Although there are instances in which Avastin is being used as first-line therapy for wet AMD, it is mostly being used in AMD "rescue" procedures, in which Macugen and/or Visudyne have failed to stabilize/improve vision and get lesions under control. Other indications have included diabetic macular edema (DME) and branch and central retinal vein occlusion (BRVO and CRVO). Once Lucentis receives FDA approval for wet AMD, we expect that Avastin use for this indication will largely disappear, given the lack of reimbursement and liability risk associated with off-label use. Avastin use in wet AMD will likely be reserved for patients that are not covered by insurance and are unable to afford Lucentis.

Anecdotally, Avastin outcomes have been consistently positive, although most clinicians that have used both Lucentis and Avastin believe that Lucentis is more effective. Those who believe that the efficacy of the two drugs is equivalent point out that much of the Avastin use

so far has been in "rescue" cases. Physicians have observed that Avastin appears to maintain efficacy over a period of about 2-3 months.

CMS is cracking down on physician reimbursement for intravitreal injections of Avastin. The cost of the drug itself is not reimbursed, although in quantities used for intravitreal injection, the cost is relatively low at \$15-75 per dose. Based on the investigational nature of intravitreal Avastin and the lack of supporting clinical data, all 17 Medicare carriers covering all 50 states have issued verbal denials of coverage, and seven carriers covering 12 states have issued written denials. Retina specialists are hoping that the reimbursement situation will improve in the coming months, supported by the near-term publication of a number of peer-reviewed articles, in *RETINA* and other journals, covering physician-led studies of intravitreal Avastin.

Macugen: The Clock is Ticking

With the outstanding clinical outcomes reported for Lucentis and positive experience with off-label Avastin, interest in Macugen among retina specialists is clearly diminishing. After one year of commercial availability, Retina specialists express overall dissatisfaction regarding Macugen's efficacy. Macugen sales in the US should hold up reasonably well until the approval of Lucentis, despite a shift of some share to offlabel Avastin and on-study Lucentis (SAILOR study). Although there have been over 5,000 injections of Avastin in the US since August 2005 and the rate of use is clearly growing, not all of these injections have been for cases of wet AMD, and liability and reimbursement concerns will prevent intravitreal Avastin from becoming a mass-market product. In many cases, Avastin is being reserved for patients that have failed to respond after several Macugen injections. Some patients are also being treated at present with Lucentis as part of the SAILOR study, but there have only been about 600 patients enrolled so far, and the study is limited to 5,000 patients.

Beyond wet AMD, the availability of low cost, off-label Avastin represents an ongoing threat to the Macugen franchise. As Macugen makes its way through clinical trials for new indications, such as DME and CRVO, promising outcomes will lead physicians to try Avastin for such indications.

How low could it go? It was suggested by some of the Retina 2006 faculty members that Macugen could see future use in wet AMD patients as chronic therapy following initial treatment with Lucentis. It is not clear to us why such a course of treatment would be chosen over continued use of Lucentis, unless unforeseen long-term

safety issues were to emerge for Lucentis. In a presentation at the JP Morgan Healthcare Conference earlier this month in San Francisco, management of OSI Pharmaceuticals stated that it had forecast a worst-case scenario for Macugen, and was comfortable that such a scenario would still be profitable and cash-flow positive for the franchise. To borrow a phrase from the 9/11 commission, this supposedly worst-case forecast may represent a "failure of imagination" on the part of OSI management.

Visudyne Sales Finally Feeling the Effects of the Anti-VEGFs

Last week, QLT, Inc. reported total worldwide Visudyne revenues for Q4-2005. Sales decelerated further as 2005 came to a close, turning in a significantly lower sequential quarter for the first time. Global Visudyne sales for Q1 to Q4 of 2005 were \$124 million, \$129 million, \$124 million, and \$108 million, representing year-over-year growth of +23%, +18%, +9%, and -13%. The deceleration has been even more pronounced in the US, where Macugen was launched in early 2005. US Visudyne sales were down y/y by 4% and 10% in Q2 and Q3-2005, respectively. Although QLT has not yet reported the US/international breakdown for Q4, domestic revenues will likely show a much larger double-digit decline in the period. The sales picture will very likely worsen for Visudyne later this year following the approval of Lucentis.

Some retina specialists at Retina 2006 expressed the view that Visudyne has a brighter future than does Macugen, given its differentiated mechanism of action.

Intravitreal Kenalog – Giving Way to that Other Off-Label Therapy

Off-label use of Kenalog, or intravitreal triamcinolone acetonide (IVTA), is fading as a "hot topic" among the retinal community. For AMD patients, IVTA has seen increasing use over the past few years in combination therapy with Visudyne/PDT, to improve efficacy and reduce the number of required PDT treatments. The shift toward Macugen (and Avastin) in 2005 and coming shift toward Lucentis in 2006 and beyond has tempered the interest in IVTA for AMD. Off-label IVTA is also used for several

other retinal indications, most notably diabetic macular edema, for which it is considered the current standard of care. However, many retina specialists are experimenting with off-label intravitreal Avastin for these indications. Early experience appears to be favorable, and most physicians believe that Avastin will prove to be safer than IVTA, which is known to cause cataracts and lead to elevated IOP/glaucoma.

Retaane Update: Enrollment in Risk Reduction Trial Coming to a Close

Alcon's drug candidate for AMD, Retaane (anecortave acetate), continues its long march toward an AMD risk-reduction indication. The company's large-scale risk-reduction study is designed to demonstrate that Retaane reduces the risk of progression of eyes with high risk dry AMD to neovascular (wet) AMD. The trial was designed to enroll 2,500 patients, and as of last week 2,531 had been enrolled at 107 sites worldwide (80 in the US). Enrollment will be closed at the end of January. This 48-month study still has a long way to go before completion of patient follow-up.

Expect Growing Interest in AMD Screening and Diagnosis

Now that there's a wet AMD treatment coming that improves vision and has the attention of physicians, there should be increasing interest in earlier disease detection, possibly through more effective screening upstream of the retina specialist. Macugen and Visudyne trials have shown that treatment is more effective when smaller, earlier lesions are treated. A lecture on early detection of AMD at Retina 2006 was introduced by course co-director Jay Duker, MD as "maybe the most clinically applicable talk of the meeting."

Surgical Advice We Can All Appreciate

The best clinical pearl from Retina 2006 came from Caroline Baumal, MD, New England Eye Center, Tufts University, Boston: Bausch & Lomb's Retisert implant for posterior uveitis costs \$18,000. It cannot be resterilized. *Don't drop the Retisert implant on the floor!* Q



Cataract and Refractive from Page 1

We view it as ironic that multifocal IOLs are experiencing a comeback at the same time that so much energy is being devoted to maximizing post-surgical visual quality. The drawbacks associated with multifocal IOLs are well known: loss of contrast sensitivity, compromise of either near or intermediate vision, and higher risk of glare and halos.

Such concerns over multifocals are contributing to growing interest in the crystalens accommodating IOL from eyeonics. Even surgeons that have opted against using crystalens are expressing interest in second generation accommodating IOLs that have the potential to deliver higher levels of accommodation while avoiding the visual compromises of multifocals. One such lens, the Synchrony dual-optic IOL from Visiogen, has recently started enrolling its pivotal US clinical trial. Updates on both the crystalens and Synchrony are provided below.

eyeonics Gears Up for More crystalens Growth in 2006

After posting record sales once again in the fourth quarter of 2005, eyeonics is preparing for more growth in 2006. The company is doubling its manufacturing capacity, and will triple its sales force in 2006, from about 35 representatives to about 100. The company has recently raised a \$16.2 million Series E round from current investors to fund the expansion, and an IPO is possible later this year.

Hawaiian Eye 2006 Program Director Richard Lindstrom, MD of Minneapolis, MN presented an update of his three-year experience with crystalens at Hawaiian Eye. Key points:

- The lens provides better intermediate vision than any monofocal or multifocal IOL, but achieves J3 near vision, not J1.
- At distance, crystalens is similar to monofocal IOLs and better than multifocals.
- crystalens generates more glare and halos than monofocal IOLs due to the smaller optic, but less than multifocals, making it the best presby-IOL for night driving.
- Dr. Lindstrom is a proponent of mixing and matching presby-IOLs based on patient feedback, and crystalens is often his first IOL choice. The lens can also be used effectively in a blended vision/monovision approach, and near vision can be enhanced using conductive keratoplasty (CK).

There is probably a multi-factorial mechanism of action, involving arching, bending, and/or tilting of the lens that induces increased coma, spherical aberration, and astigmatism that enhances depth of focus.



eyeonics crystalens

Visiogen Synchrony

US Trial Enrollment Begins for Synchrony Dual-Optic IOL

Early success for the initial wave of presbyopiacorrecting IOLs is sparking increased interest in the next wave of technologies. Of particular interest are accommodating IOLs that can provide greater amplitude of accommodation. The leading product candidate today is the Synchrony dual-optic accommodating IOL from privatelyheld Visiogen, Inc. US pivotal trial enrollment began in November, shortly after the company's new pre-loaded inserter was approved by the FDA for incorporation into the trial protocol. In initial studies, the injector induced significantly less surgery-related astigmatism versus forceps insertion.

FDA approval is targeted for 2008. The trial has already enrolled multiple patients in multiple sites. About 270 Synchrony IOLs have been implanted outside the US. Dualoptic IOLs can deliver a higher level of accommodative amplitude than single-optic lenses, and Synchrony has maintained 3D of accommodative power even two years post-implant. In patients implanted outside the US with the latest version of the product, with distance correction in place, 100% of eyes have achieved visual acuity of 20/40 or better at distance and near, and 96% have achieved 20/40 or better at intermediate distance. Even without correction, 100% have achieved 20/40 or better near vision.

Bausch & Lomb Foregoes Multifocals, Forges Ahead with Accommodating IOLs

Bausch & Lomb provided an update on its efforts in the presby-IOL field at its analyst/investor meeting in December and at the JP Morgan Healthcare Conference in January. As one of the "big three" IOL manufacturers, Bausch is conspicuously absent from the current market for presbyopia-correcting IOLs. The company states that it made a conscious decision to leapfrog multifocals and go straight to accommodating technology, although this would appear to be a strategic miscalculation given the lower technical barriers and current commercial success of the new multifocals.

Bausch's primary entry in the accommodating IOL field is its Sarfarazi dual-optic lens, which appears to be at least a year behind the Visiogen Synchrony. The Sarfarazi lens has been implanted in humans, but the design has not yet been finalized, so the pivotal trial has not yet begun. Bausch hopes to reach this step by later in 2006. A European launch is targeted for the end of 2007, with a US launch possible 12-18 months thereafter (2009).

Bausch & Lomb has also developed or acquired a singleoptic accommodating IOL with 1D of accommodative amplitude. This product would be a direct competitor to the eyeonics crystalens. Bausch plans to launch this lens in Europe and Asia by the end of 2006 or early 2007. At Hawaiian Eye, we heard that Bausch may have licensed the Akkommodative 1CU from HumanOptics AG of Germany.



If this is true, it is not clear why the European launch is not scheduled until about one year from now.

The "Mix & Match" Debate Rolls On

The question of whether surgeons should consider mixing and matching presbyopia-correcting IOLs picked up in Wailea where it left off at the AAO in Chicago. A

number of surgeons have reported favorable outcomes after implantation of one of the three approved lenses in a patient's first eye and a different lens in the second eye.

Alcon is clearly the driving force behind the arguments against mixing and matching. The case against mixing and matching seems to be based more on commercial than on clinical arguments, driven by Alcon's reluctance to concede a single implant to the competition. While it is true that there is not yet a strong body of clinical evidence supporting the mix-and-match approach, neither is there a body of evidence showing that it is bad for patients, and most of the anecdotal evidence so far appears to be positive. One of the arguments against mixing presby-IOLs is that if a patient is unhappy with his or her visual outcome, it is more difficult to explain why two different IOLs were used. This would appear to be a manageable situation, driven by good physician-patient communication.

Aspheric IOLs – Improving Post-Cataract Visual Quality

There is a healthy debate (less name calling than in the presby-IOL debate) regarding the relative merits of the three major aspheric IOLs on the market. These lenses address the fact that as the crystalline lens ages, it loses its negative spherical aberration (SA), which in the young eye counteracts the positive SA of the cornea and contributes to a high quality image. As the SA of the lens increases and eventually becomes positive, visual quality is negatively impacted, with increases in glare effects and decreases in contrast sensitivity. Conventional IOLs have also featured positive SA, and have failed to address this visual quality problem. As cataract patients become more demanding with regard to post-surgical uncorrected visual acuity and quality, these IOLs should continue to grow in popularity.

The new aspheric IOLs follow two basic approaches:

IOLs that feature zero SA, neither adding to nor subtracting from the positive SA of the cornea. The Bausch & Lomb SofPort AO lens falls into this category. The key advantage of this approach is that IOL placement is very forgiving with respect to decentration, tilt, and variation in pupil size. While this lens would leave some positive SA in the eye, some surgeons believe that this is desirable. Also, this lens might be a good choice in patients with a prior LASIK procedure, given the possibility that the ablation might have been imperfectly centered.

• IOLs that feature negative SA, to counteract the cornea's positive SA. The AMO Tecnis lens and Alcon AcrySof IQ lens fall into this category. While surgical placement is less forgiving with respect to tilt and decentration, this approach should provide superior visual quality if the IOL is properly aligned within the eye.

A New Paradigm for Cataract and Refractive Surgery Practices

The idea that cataract surgery is a form of refractive surgery is not a new one, and new surgical technologies for presbyopia are certainly blurring the lines between the two specialties. In a symposium on conductive keratoplasty (CK), Dr. Daniel Durrie of Kansas City outlined an approach for cataract and refractive surgeons that borrows from other ophthalmic subspecialties that traditionally follow patients over a longer period of time.

Traditionally, the surgeon-patient relationship for both cataract and refractive surgeons has consisted of a relatively brief encounter, culminating in the performance of a single surgical procedure on each eye. If an enhancement is needed, it is usually included in the original procedure fee. Dr. Durrie describes this as a "catch and release" model of patient acquisition.

With the emergence of treatments for presbyopia, a shift to an "acquire and hold" approach to patient lifecycle management is warranted. The best source of presbyopia surgical candidates may be a refractive practice's own satisfied LASIK patients. Dr. Durrie suggests three basic elements of this approach: (1) A "starter procedure," which will be LASIK in most instances; (2) broadening practice scope to incorporate follow-on procedures and enhancements, such as CK, presbyopic IOLs, and corneal inlays; and (3) a business model that charges for such follow-on procedures. These procedures can be discounted to reward patient loyalty, but should not be included in the

initial procedure fee.

These concepts are not new to ophthalmology, just to cataract and refractive surgeons; retina, glaucoma, and oculoplastic specialists already incorporate these concepts of patient lifecycle management into their practices.

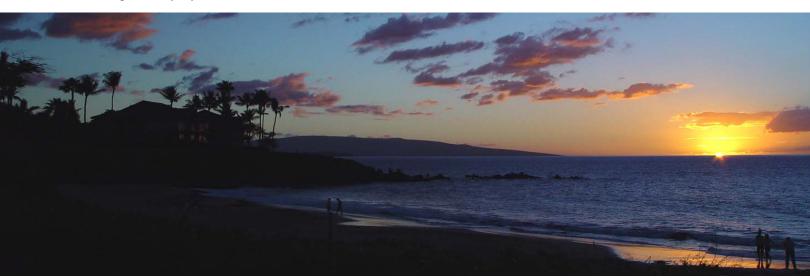
Dr. Durrie is already finding that this approach to patient marketing and education is helping to drive some LASIK procedure volume, giving patients a reason to choose a comprehensive practice over those that follow a "catch and release" LASIK-only model.

Additional words of wisdom on the practice management front came from Dr. Rosa Braga-Mele of Toronto, who made a case for why it so important for today's refractive surgeons to be nice to their patients (yes, it matters). With the proliferation of surgical options available, particularly for presbyopia, it is critical for surgeons to understand their patients' interests, recreational activities, work environment, and expectations regarding post-surgery vision.

Laser Vision Correction Procedure Trends: A Good Finish to 2005, Mixed Signals for 2006

LASIK surgeons at Hawaiian Eye generally reported a strong finish to 2005. For many, LASIK volumes in the third quarter of 2005, and even the early part of the fourth quarter, were down versus the same months of 2004. However, December volumes were strong, resulting in overall Q4 volumes that were even with or slightly above those of O4-2004.

The outlook for 2006 is neither strongly positive nor strongly negative so far. January is always a very busy month in the refractive surgery business, due to the effect of flexible healthcare spending accounts. As such, January



volumes are usually more representative of practice capacity than of any real year-over-year changes in demand. At this time of year, surgeons look to their February and March bookings as leading indicators of demand for the coming year. Some surgeons with whom we spoke at Hawaiian Eye reported very strong bookings for the next two months, and some reported a few more openings on the schedule than at this time last year. Overall, this would suggest volumes for Q1-2006 that are flat to slightly higher versus Q1-2005.

Alcon's LADAR 6000 System Set for Near-Term Launch

Alcon's LADARVision 4000 excimer laser system,

despite the many innovations that it has introduced into the market, has always been lacking in the areas of surgical efficiency and ergonomics. Alcon is addressing at least some of these issues with the coming release of the LADAR 6000 system. An approvable letter for this system was issued in November, and full FDA approval and US launch are expected shortly.



Although the overall layout of the LADAR 6000 system is similar to prior versions, retaining the center post that connects the laser head to the patient bed, the system incorporates 80% new components. As such, it is not an upgrade but a completely new laser (that is designed to accommodate future upgrades). We have heard from a number of Alcon users that the company intends to price the LADAR 6000 attractively to existing LADARVision customers in order to encourage rapid switching. Users will benefit from a more efficient system, and Alcon hopes to benefit from lower service/maintenance requirements and higher procedure volumes and procedure-based revenues. We have also heard that a completely new excimer laser platform is under development at Alcon, which is likely several years away from commercialization.

Features and benefits of the LADAR 6000 include:

- Laser frequency about 50% faster than before. A 10D ablation will be completed in less than 60 seconds, versus a previous ablation time of about 80 seconds.
- Improved surgeon ergonomics, including a better graphical user interface and workspace, and an enhanced illumination system.
- Automated registration system that allows simplified matching of the measured wavefront with the eye during surgery, improving the efficiency of the process. Future versions will align wavefront data and ablation patterns, and compensate for cyclotorsion, based on recognition of blood vessels in the sclera, eliminating the need for marking the eye on the day of surgery. A dilated pupil during surgery will still be required, because the fundamental approach to eye tracking has not changed.
- Reduced service and maintenance requirements, including gas fill on a weekly, not daily, basis. Q

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