BUSINESS PERSPECTIVE

Ophthalmic leaders discuss trends, new treatment options, and compliance issues.

BY STEPHEN DAILY, EXECUTIVE EDITOR, NEWS, BMC

As ophthalmic companies search for new and innovative ways to solve unmet needs, technological advances are playing a direct role in the types of drugs and devices being developed and the way treatment regimens are administered.

Although the focus ultimately remains on improving visual acuity, the ophthalmic industry has devoted more resources in recent years to drugs and devices that achieve this objective in a faster, safer, and less invasive manner.

The FDA's recent approval of small-incision lenticule extraction using the VisuMax laser (Carl Zeiss Meditec) as well as microinvasive glaucoma surgery (MIGS) devices (iStent Trabecular Micro-Bypass Stent [Glaukos] and Cypass Micro-Stent [Alcon]), corneal inlays (Kamra [AcuFocus] and Raindrop Near Vision Inlay [ReVision Optics]), and corneal collagen cross-linking (KXL System; Avedro) has provided surgeons with effective new treatment options. In addition, drug candidates that employ new mechanisms of action, along with sustained-release drug delivery tools, aim to address the problem of poor adherence to prescribed medical therapy.

As part of *CRST*'s series on the future of innovation in ophthalmology, we spoke with leaders of ophthalmic companies that represent different specialty areas to discuss which trends they expect to see in ophthalmology over the next decade.

JAMES MAZZO
Global President of Ophthalmology
Carl Zeiss Meditec

JOSEPH BOORADY, OD
President and CEO
TearScience

VINCE ANIDO JR, PHD
Chairman and CEO
Aerie Pharmaceuticals

MARK BAUM
Founder and CEO
Imprimis Pharmaceuticals

***CRST*: When considering the future of ophthalmic technology and innovation, where do you believe the next decade will take us? What trends will change the way patients are treated?**

James Mazzo: I think, anytime you look at a trend, you have to look at what are the demographics. Obviously, you have an aging population, and you have the baby boomer generation growing older as well. I look at categories such as presbyopia, retina, glaucoma, and dry eye. Why? Unmet needs are going to affect those populations, and companies are going to invest in them. (See *Watch It Now* for an interview with Mr. Mazzo.)

The one I just started talking about in a previous session (at the Ophthalmology Innovation Summit) is software

WATCH IT NOW

James Mazzo discusses how changing demographics are going to affect the future of ophthalmic technology and innovation.

development. As we start to look at the technologies—and there are large pieces of capital equipment sitting in a doctor's office—the last thing [physicians] are going to want to do is remove that capital. So, can we start to develop software in which we can just update that piece of capital equipment? I look at it from a category of demographics and unmet needs in treatment. I also look at how do we take advantage of what we've already created and make it better? That would be software.

Joseph Boorady, OD: Thinking about technology and innovation in the next decade, I believe we will see continued advances in cataract and refractive surgery, including better procedures and technology to improve outcomes and visual performance. We will also see advancements in MIGS devices for glaucoma and exciting innovations in drugs and delivery systems for retina. But, I remain most bullish on the advances in dry eye and meibomian gland dysfunction, where TearScience has contributed. All of the procedures and technologies just mentioned require a healthy ocular surface to provide stable vision and comfort from the common onset of [dry eye disease] symptoms that accompany these procedures and conditions. A healthy tear film also provides an important barrier to infection. (See *Watch It Now* for an interview with Dr. Boorady.)

Vince Anido Jr, PhD: We've had a tremendous amount of investment going into ophthalmology over the last 7 to 10 years, and so it's all now coming to fruition. You've got new chemical entities, like ours, coming out in terms of new treatments for glaucoma. We see other companies

> "Single drug bottles of eye drops will go the way of the proverbial horse and buggy."
> —Mark Baum

doing that as well. We've seen a huge amount of venture investing going into devices, and whether they're MIGS or whether they're drug delivery systems, they are all trying to solve various different problems. I think all of those are now just coming to fruition.

We see a couple of the MIGS [devices] out on the marketplace now. We expect a third [MIGS device] coming out over the next few years. We expect new drugs to come out over the next year or 2. All of that is just simply going to continue fueling a lot of the R&D investment. Whether it's the venture guys that are doing it or whether it's pharmaceutical companies that are doing it or some of the start-ups like us and Glaukos or Ophthotech, we'll continue to be able to get funding so that we can continue to look for new solutions that we think will help the patients.

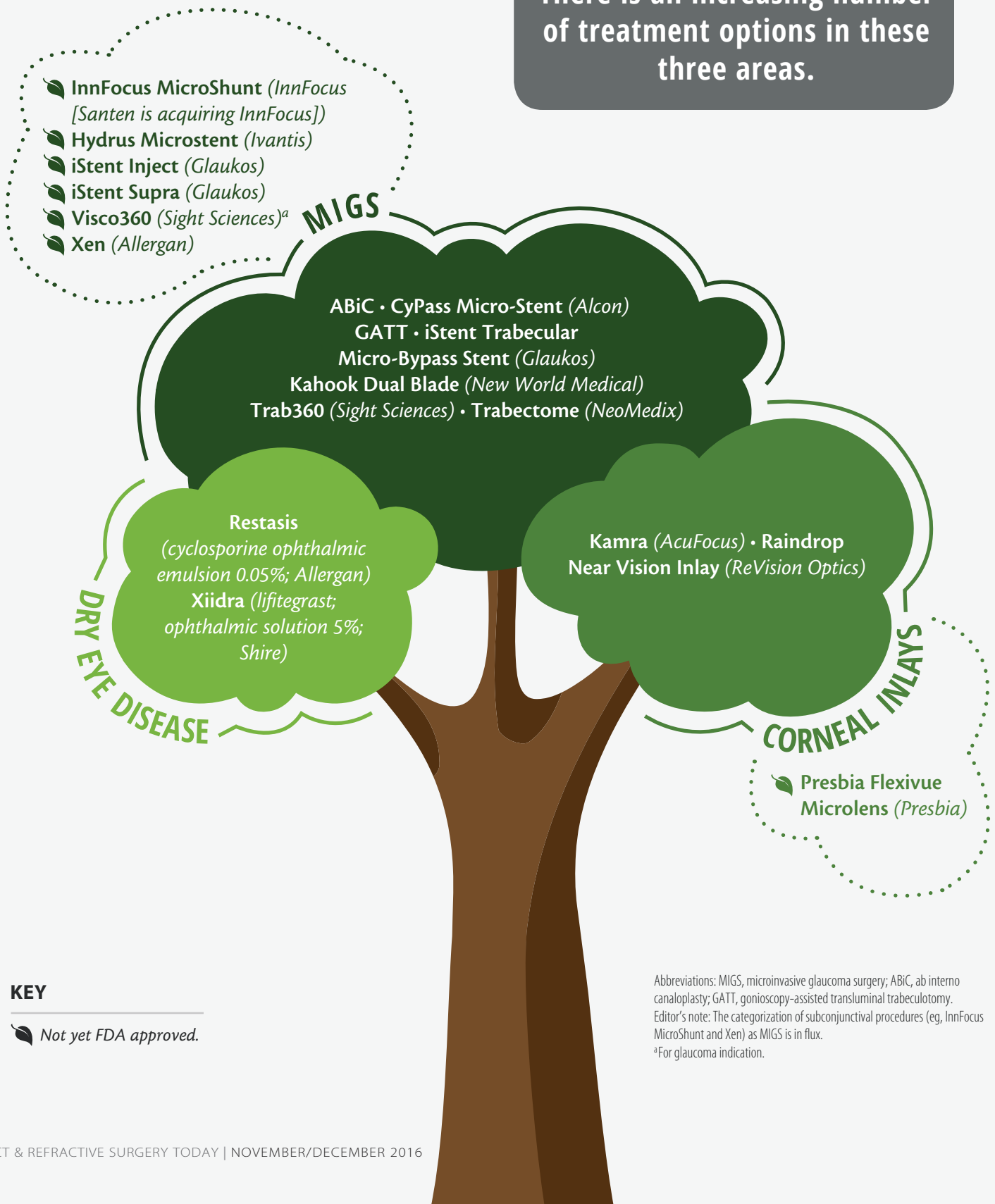
Mark Baum: I believe that, generally, single drug bottles of eye drops will go the way of the proverbial horse and buggy. New ways of delivering postsurgery prophylaxis against inflammation and infection will dominate the cataract surgery market. New chemistries of combinations of medicines that ease the burden of patient compliance will continue to gain momentum. New delivery modalities will also proliferate outside of a front-of-the-eye practice. Companies that have invested in new technologies will have the opportunity to thrive, and others that have not innovated or that have fought to stop progress will be penalized.

***CRST*: Do you believe there's an emphasis on moving patients along sooner to a surgical solution for diseases, or do you believe drug regimens will remain a focus?**

Mazzo: To address your question, let's look at retina. The only way a drug is going to get to the back of the eye is through a device. I don't know if it's surgical, but I think a drug delivery type of mechanism is going to be the future. Also for dry eye, the way that you really get through the tear film and get [the treatment] to where it needs to be is going to be some type of a device.

THE GROWTH OF COMPETITION

There is an increasing number of treatment options in these three areas.



KEY

Not yet FDA approved.

Abbreviations: MIGS, microinvasive glaucoma surgery; ABiC, ab interno canaloplasty; GATT, gonioscopy-assisted transluminal trabeculotomy.
Editor's note: The categorization of subconjunctival procedures (eg, InnFocus MicroShunt and Xen) as MIGS is in flux.
[a]For glaucoma indication.

> "You're not going to be able to get rid of drugs just because you've got a surgical intervention."
> —Vince Anido Jr, PhD

It's going to be a combination of both pharmaceutical and devices. That's why I'm pleased at Zeiss; we obviously are leaders in devices, so we can look at our devices to be complementary to the drugs. Then, of course, before you get to any treatment, you've got to diagnose it. I would say you should be careful of trying to treat before you diagnose, as you could mistreat and that's where you have escalating costs and unhappy patients. Let's get the diagnostic machines ready and then be ready to treat.

Boorady: There are certainly elements of disease that are best served by surgical procedures and devices. In arterial disease, drug agents are essential, but when blockage is present, a stent is needed. If you were to rely on drugs first, you might lose the patient. I do think there are similarities with many ophthalmic conditions, where intervening with devices or surgery earlier in the disease process should be an emphasis. Clinicians have newer technologies that can safely get directly to the root of the problem while also addressing systemic processes and downstream sequelae with appropriate drugs.

The LipiFlow [TearScience] is a great example. [Meibomian gland dysfunction] was a disease that, for decades, was treated with heat and massage from the outside of the lid, requiring potentially unsafe amounts of pressure on the globe with only [a] marginal, fleeting effect. Modern engineering was tapped to effectively heat the inner lid directly adjacent to the glands. LipiFlow then applies gentle pressure simultaneously to express blockage and potentially necrotic tissue with a phased peristaltic pressure profile while protecting the delicate structures of the cornea, globe, and lid. The combination of ingenious patented concepts, new materials, and classic lens design safely removes obstruction by a well-understood mechanism of action.

LipiFlow has now been shown to provide patients with a year of improvement from a single 12-minute procedure in a large, randomized multicenter trial.[1] It solves an issue in need of a mechanical solution and in turn maximizes [the] effectiveness of drugs and supplements thereafter.

WATCH IT NOW

Joseph Boorady, OD, shares why he is bullish on the future of dry eye and meibomian gland dysfunction technologies.

With the advent of MIPS [Merit-Based Incentive Payment System] and other quality metrics, better patient outcomes earlier in disease processes will be a necessity. This will especially be the case with self-pay procedures where physicians provide effective and lasting treatments and control pricing—procedures that will provide great outcomes while at the same time contribute to practice growth.

Anido: If you focus only on where the venture investing is going, you'd think, "Oh my God, everything is going to some sort of a surgical solution. Right?" There's an awful lot of information about the MIGS and drug delivery systems. The facts are that, while all those are quite effective, we've never seen a therapeutic market go to zero as a result of surgical intervention. If you take a look at the cardiology space and things like that, certainly, the pharmaceutical component of it continued to move forward. We don't think that it's going to have a negative impact on ophthalmic pharmaceutical products. In fact, all of these drugs, while they do something positive for the patient, they don't really treat the underlying disease. For example, one we know well in glaucoma, a lot of these [devices] don't treat the fibrosis and the trabecular meshwork, so you're not going to be able to get rid of drugs just because you've got a surgical intervention. (See *Watch It Now* for an interview with Dr. Anido.)

Baum: Ophthalmologists will always make the best call for their patients based on the respective individual needs of the patient. More and more care will be delivered by

WATCH IT NOW

Vince Anido Jr, PhD, explains why it is necessary for the therapeutic market to complement surgical intervention.

ophthalmologists in their office—whether it is a surgical intervention or the administration of a drug regimen. My hope is that power is restored to the ophthalmologist as a "giver of care" and that middle parties lose power over decisions connected to the care of patients.

CRST: In what ways are companies focusing on decades-old patient compliance issues?

Mazzo: I agree that patient compliance has been, and will continue to be, a significant issue when treating patients with chronic diseases. To help, our effort at Zeiss is to make it easier for clinicians to diagnose and manage patients and, equally important, to aid clinicians in patient[s'] education about their disease and its progression. Diagnostic images and exam-to-exam changes can be used to consult with patients about their condition and need for treatment and/or therapy. Simple, but impactful, images as well as careful counseling holds one of the keys to improving patient compliance.

Boorady: We're seeing innovation to solve for patient compliance in several areas. There are intraoperative injections and new drug and therapy delivery devices in the works to overcome the shortcomings of patient noncompliance. TearScience is highly focused on compliance issues. For over 100 years, the efficacy limitations inherent with warm compresses are compounded by horrific compliance. Compliance was right behind efficacy as the motivation for the development of LipiFlow. After years of experimenting

> "Compliance ... will continue to be a significant issue when treating patients with chronic diseases."
>
> —James Mazzo

with multiple heat and energy sources to safely remove meibomian gland obstruction, including [infrared, radio frequency,] ultrasound, heat paddles, steam, and laser, to name a few, we realized that just heating the meibomian glands did not remove obstruction, and in fact, within seconds after the heat source was removed, the blockage recongeal[ed]. It was only with inner lid heat and simultaneous expression that we achieved significant long-term results and thereby eliminate[d] compliance challenges.

Anido: All of us worry about compliance, and so from a drug perspective, we try to get everything down to a once-a-day product. We think that that's where you have the highest compliance. For example, we have a combination of our drug Rhopressa (netarsudil) with latanoprost, both of those once a day, we call Roclatan (netarsudil-latanoprost), because then we think you'll get pretty good compliance when you have two drugs in one bottle and the patient doesn't have to have that second drop. Certainly, we see a lot of drug delivery systems that are out there, whether they're surface delivery systems like the punctal plugs or the rings or the ones that are injected or inserted, that we think will enhance compliance to some degree.

At the end of the day, if you could focus it only on once a day, or if you can bypass that and put it in the surgeon's hands to be able to do it intracamerally or to the back of the eye—a solution with a long-acting device of some sort—we think all that will enhance the compliance.

Baum: Our mission is 100% committed to high-quality innovation but also access and affordability. We fulfill our mission by combining medicines into new combination topical and injectable formulations. The upshot for the patient is that we relieve them and their physician of compliance challenges that we all know are pervasive. We also do this while saving patients and the government a lot of money. It's a true win-win for everyone. ■

1. Blackie CA, Coleman CA, Holland EJ. The sustained effect (12 months) of a single-dose vectored thermal pulsation procedure for meibomian gland dysfunction and evaporative dry eye [published online ahead of print July 26, 2016]. *Clin Ophthalmol*. doi:10.2147/OPTH.S109663.