

# LONGER-TERM DME OUTCOMES PREDICTED BY EARLY RESPONSE TO ANTI-VEGF THERAPY

Eyes with diabetic macular edema (DME) that have an early response to anti-VEGF treatment, measured as a reduction in central retinal thickness (CRT), will have significant response to treatment by 3 months, a small retrospective study found.<sup>1</sup>

The single-center, interventional case series was published in the *Journal of Vitreoretinal Diseases*. Researchers identified 107 patients with DME treated with repeated anti-VEGF injections. Of these patients, 34 (40 eyes) met all study inclusion criteria. Patients who received three consecutive monthly injections with the same anti-VEGF agent were included; patients who were treated for DME in the preceding 3 months with any form of anti-VEGF therapy were excluded.

Within the first month, visual acuity (VA) in all eyes improved from  $0.60 \pm 0.37$  logMAR (Snellen 20/80) to  $0.53 \pm 0.36$  logMAR (Snellen 20/68;  $P = .030$ ). VA continued to improve to  $0.47 \pm 0.42$  logMAR (Snellen 20/59) and

$0.40 \pm 0.33$  logMAR (Snellen 20/50) by 3 months ( $P = .010$ ) and 12 months ( $P < .001$ ), respectively. According to the researchers this improvement seemed to correlate with significant reduction in CRT noted at all time points measured.

The investigators sought to identify a marker for better response to anti-VEGF therapy. They found that patients who had a greater than 15% reduction in CRT at 1 month would go on to have a 25% reduction at 3 months (sensitivity, 0.75; specificity, 0.92; positive predictive value, 0.86; negative predictive value, 0.85). This cutoff correctly identified 16 of 16 responders and 18 of 24 poor responders to anti-VEGF therapy.

The study researchers concluded that “This approach is readily available, cheap, and noninvasive and can be combined with other measurable parameters to drive complex management of patients with DME.”

1. Shah AR, Yonekawa Y, Todorick B, et al. Prediction of anti-VEGF response in diabetic macular edema after 1 injection [published online ahead of print February 1, 2017]. *Journal of Vitreoretinal Diseases*.

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### Ranibizumab Prefilled Syringe Available

Genentech announced that US physicians will now have access to ranibizumab (Lucentis, Genentech) in a prefilled syringe (PFS).

The PFS will allow physicians and staff to eliminate several steps in preparation prior to administration, according to the company. These steps include disinfecting the vial, attaching a filter needle, drawing medication from the vial using the needle, and removing the filter needle from the syringe and replacing it with the injection needle.

EyewireTV spoke with David Eichenbaum, MD, about the PFS. He commented that the PFS’s efficiency makes it a preferable method of delivering ranibizumab. You can watch his interview with EyewireTV at [bit.ly/genentech317](http://bit.ly/genentech317).

### ERRATUM

In the top news story of our January/February issue (“FDA Approved First Anti-VEGF Agent for Myopic CNV”) we mistakenly reported the wrong figures for the average change in ETDRS letters at 3 months in the RADIANCE study. The sentence should have read, “Patients in the ranibizumab groups demonstrated improvements of 12.1 and 12.5 ETDRS letters at month 3 compared with improvement of 1.4 ETDRS letters in the PDT group ( $P < .001$ ).” This information has been updated in the online version ([bit.ly/117news](http://bit.ly/117news)) of this article. *Retina Today* apologizes for the error.

## FDA Orphan Drug Status Given to GenSight Biologics' GS030 for RP

The US Food and Drug Administration (FDA) granted orphan drug designation to GenSight Biologics' product candidate GS030 for the treatment of patients with retinitis pigmentosa (RP), the company announced. GS030 received both orphan drug designation and advanced therapy medicinal product classification in Europe in September 2016.

GS030 is expected to benefit patients in the early stages of RP. The product candidate leverages GenSight's optogenetics technology platform, which restores vision to patients by using gene therapy to introduce a gene encoding for a light-sensitive protein into specific target cells in the retina to make them responsive to light. An external wearable medical device to stimulate the transduced cells is being developed to amplify the light signal and enable vision restoration.

According to GenSight, GS030 is undergoing a Good Laboratory Practice regulatory toxicity study and is expected to enter clinical investigation with a phase 1/2 clinical trial in patients with RP in the third quarter of 2017.

GenSight Biologics receives FDA orphan drug designation for GS030 in retinitis pigmentosa [press release]. GenSight Biologics. January 31, 2017. [www.gensight-biologics.com/uploads/Modules/InvestorNews/gensight-biologics\\_pr\\_gs030-us-odd\\_01302017\\_vdef.pdf](http://www.gensight-biologics.com/uploads/Modules/InvestorNews/gensight-biologics_pr_gs030-us-odd_01302017_vdef.pdf). Accessed March 3, 2017.

## Aura Biosciences Received FDA Permission to Study AU-011 for Treatment of Ocular Melanoma

The FDA cleared an investigational new drug (IND) application for Aura Biosciences' light-activated AU-011 in ocular melanoma, enabling the company to begin initial clinical testing of this targeted therapy.

AU-011 consists of viral nanoparticle conjugates that bind selectively to cancer cells in the eye. After intravitreal injection, the drug is activated with a laser, and its necrotic mechanism of action selectively destroys tumor cells while sparing health cells.

Aura founder and chief executive officer (CEO) Elisabet de los Pinos, PhD, commented, "Our hope is that AU-011 could be used to treat small primary melanomas early, with the potential to eliminate the tumor and preserve vision for patients."

Aura is enrolling participants in a phase 1b, open-label, single ascending dose clinical trial to evaluate the safety, immunogenicity, and preliminary efficacy of two dose levels of the drug for the treatment of small-to-medium primary ocular melanoma.

Aura Biosciences receives FDA clearance of investigational NDA for light-activated AU-011 for the treatment of ocular melanoma [press release]. Aura Biosciences. February 6, 2017. [www.aurabiosciences.com/news-archive/2017/2/5/aura-biosciences-receives-fda-clearance-of-investigational-new-drug-application-for-light-activated-au-011-for-the-treatment-of-ocular-melanoma](http://www.aurabiosciences.com/news-archive/2017/2/5/aura-biosciences-receives-fda-clearance-of-investigational-new-drug-application-for-light-activated-au-011-for-the-treatment-of-ocular-melanoma). Accessed March 3, 2017.



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### Novartis: Alcon Spinoff, IPO Could Be on the Horizon

Novartis is considering a spinoff or initial public offering (IPO) of the company's Alcon unit in an effort to maximize shareholder value following a 3% decrease in sales in the Alcon division, the company announced.

The drop in sales was blamed on two aspects of anterior segment surgery. Revenue in cataract and refractive surgery equipment fell in 2016, and competitive pressures in the intraocular lens market also had an effect, according to the company.

EyewireTV broadcast a portion of a talk by Joseph Jimenez, CEO at Novartis, delivered at an earnings meeting with investors. To view EyewireTV's coverage of the story and see Mr. Jimenez's talk, visit [bit.ly/alcon317](http://bit.ly/alcon317).

## Enrollment Completed in Phase 3 Trials of Lampalizumab

Genentech has completed enrollment in two large phase 3 clinical trials, Chroma and Spectri, investigating the efficacy and safety of lampalizumab in reducing the progression of geographic atrophy (GA) lesions secondary to age-related macular degeneration (AMD).

The two identical, double-masked, sham-controlled studies have enrolled 1,881 patients at nearly 300 locations in more than 20 countries. For both studies, the primary endpoint is the mean change in GA lesion area at 1 year, comparing treatment to sham, with a planned overall treatment duration of 2 years. Secondary endpoints assess visual function changes.

Chroma and Spectri use assessments including low-luminance visual acuity, microperimetry, reading speed, and patient-reported outcomes, in addition to BCVA, to comprehensively measure visual function outcomes.

## Johnson & Johnson Acquisition of AMO Complete

Johnson & Johnson has completed the all-cash \$4.325 billion acquisition of Abbot Medical Optics (AMO), which includes ophthalmic products in three areas of patients care: cataract surgery, laser refractive surgery, and consumer eye health.

The combined organization will operate under the brand name Johnson & Johnson Vision, the parent company announced.

Johnson & Johnson completes acquisition of Abbott Medical Optics [press release]. Johnson & Johnson. February 27, 2017. [www.prmnewswire.com/news-releases/johnson-johnson-completes-acquisition-of-abbott-medical-optics-300413727.html](http://www.prmnewswire.com/news-releases/johnson-johnson-completes-acquisition-of-abbott-medical-optics-300413727.html). Accessed March 3, 2017.

## Clearside Biomedical Enrolls First Patient in Phase 3 RVO Trial, Redirects Resources Toward DME Program

Clearside Biomedical enrolled the first patient in its phase 3 SAPPHIRE clinical trial of Zuprata (formerly CLS-TA) for the treatment of macular edema associated with retinal vein occlusion, the company announced.

SAPPHIRE is a multicenter, randomized, masked, controlled trial to assess the efficacy and safety of suprachoroidally administered Zuprata, Clearside's proprietary suspension formulation of the corticosteroid triamcinolone acetonide, used together with intravitreally administered aflibercept (Eylea, Regeneron). Patients in the combination treatment arm will receive suprachoroidal triamcinolone with intravitreal aflibercept at the beginning of the trial, intravitreal aflibercept alone at week 4, and suprachoroidal triamcinolone with intravitreal aflibercept at weeks 12 and 24. Patients in the control arm will receive intravitreal aflibercept alone at the beginning of the trial and follow-up treatments of intravitreal aflibercept alone

every 4 weeks through week 24. The primary objective will be to determine the proportion of patients in each arm with a BCVA improvement of at least 15 letters from baseline at 8 weeks after initial treatment.

In other news, Clearside initiated a strategic realignment of its research and development resources from its preclinical development program for axitinib for the treatment of wet AMD toward its ongoing clinical development program for the treatment of DME with Zuprata. The company plans to continue to investigate axitinib and other compounds for the treatment of wet AMD, but it no longer expects to submit an IND application to the FDA for the drug.

## IBM's Watson Learning to Recognize Retina Abnormalities

Investigators at IBM Research have trained a research version of its Watson computer system to recognize abnormalities in retina images. The research began in 2015 and has recently focused on streamlining some of the manual processes used by doctors in screening patients for retinal disease.

Researchers applied deep learning techniques and image analytics technology to 88,000 deidentified retina images accessed through EyePACS to analyze key anomalies of the eye. Results to date have demonstrated Watson's ability to accurately measure the cup-to-disc ratio, a key sign of glaucoma, with statistical performance as high as 95%. Watson has also been trained to distinguish between left and right eye images with up to 94% confidence. This is important for downstream analysis and for the development of effective treatment programs.

IBM Research expects results to continue to improve over time as the technology expands to detect features of other eye diseases such as diabetic retinopathy and AMD. ■

IBM Research is training Watson to identify eye retina abnormalities [press release]. IBM Research. February 21, 2017. [www-03.ibm.com/press/us/en/pressrelease/51671.wss](http://www-03.ibm.com/press/us/en/pressrelease/51671.wss). Accessed March 3, 2017.

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### Robot Assists With RVO Surgery

Surgeons used a robot to perform surgery on a patient with retinal vein occlusion (RVO), according to a press release from University Hospitals Leuven and the University of Leuven, Belgium.

The robot, designed by engineers from the mechanical engineering department at the University of Leuven, uses a 0.03 mm needle to inject thrombolytic drug into the retinal vein of a patient with RVO. The needle is guided by a surgeon until the surgeon locks the robot, at which point the needle and the eye are stabilized, allowing the surgeon to inject ocriplasmin (Jetrea, Thombogenics) in a controlled fashion.

Tune in to EyewireTV to learn more about the procedure and see a wet lab demonstration of the surgery. Visit [bit.ly/belgium317](http://bit.ly/belgium317) and view the video from the 3:45 mark.