

To: Retina Specialists  
From: Caroline Bauman, MD, CMO <apellismedical@apellis.com>

Subject: Over 510,000 SYFOVRE® (pegcetacoplan) Injections, New Tissue Preservation Data

March 7, 2025

SYFOVRE® (pegcetacoplan injection) is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

### **SELECT SAFETY INFORMATION**

SYFOVRE is contraindicated in patients with ocular or periocular infections, in patients with active intraocular inflammation, and in patients with hypersensitivity to pegcetacoplan or any of the excipients in SYFOVRE. Systemic hypersensitivity reactions (e.g., anaphylaxis, rash, urticaria) have occurred.

**Please see additional Important Safety Information below.**

Dear Retina Community,

New data was presented at the [Macula Society](#), [Hawaiian Retina](#), and [Angiogenesis 2025](#), which included data on increasing effects of SYFOVRE through 4 years of continuous treatment.

Highlights include:

- 3.16 mm<sup>2</sup> of retinal tissue preserved with SYFOVRE monthly in nonsubfoveal GA (vs. projected sham at 48 months, post hoc)
- AREDS vitamins showed no benefit on overall GA progression or growth towards the fovea (OAKS & DERBY at 24 months, post hoc)

For full presentations, visit the [Apellis Medical Hub](#).

**What is 3.16 mm<sup>2</sup>?**



With EARLY treatment  
**3.16 mm<sup>2</sup> Retinal  
Tissue Preserved**

Retinal tissue preserved is the change from baseline in total area of GA lesion(s) vs. projected sham at month 48 in a post hoc analysis of study subjects with nonsubfoveal lesions. Image on the right is an image of nonsubfoveal lesion ~3.16 mm<sup>2</sup> in area. SYFOVRE every other month preserved 2.7 mm<sup>2</sup> of retinal tissue at month 48 in an identical analysis. Delayed treatment with SYFOVRE in patients with NSF GA [sham observed patients that received no treatment for the first 24 months and then crossed over to active treatment for the second 24 months] preserved 1.10 mm<sup>2</sup> of retinal tissue vs. 3.16 mm<sup>2</sup> in the early treatment group that received 48 months of continuous monthly treatment (post hoc).

SYFOVRE showed increasing efficacy through 4 years when comparing the first 24 months of SYFOVRE treatment with the second 24 months of SYFOVRE treatment (post hoc). SYFOVRE offers flexible dosing frequency with as few as 6 injections per year. Additionally:

- As of December 31st, 2024,
  - **Over 510,000 SYFOVRE injections** and **over 99,000 first injections** estimated to have been administered across real-world and clinical trials.<sup>1,2</sup>
  - Retinal vasculitis has been reported following SYFOVRE injection and appears to be a first injection phenomenon with a rate of ~1/4,000 per first injection.

We remain committed to supporting your treatment decisions with real-world evidence. This body of evidence continues to grow with presentations at major congresses throughout the year. Thank you for your continued collaboration.

## **ABOUT OAKS AND DERBY**

OAKS (n=637) and DERBY (n=621) are Phase 3, multicenter, randomized, double-masked, sham-controlled studies comparing the efficacy and safety of SYFOVRE with sham injections across a broad and heterogeneous population of patients with geographic atrophy (GA). Treatment with both monthly and every other month SYFOVRE reduced GA lesion growth with increasing treatment effects over time. In all GA patients regardless of lesion location, SYFOVRE reduced GA growth by 18% and 22% monthly, 17% and 18% every other month over 24 months in OAKS and DERBY, respectively. There was no statistically significant difference between SYFOVRE arms and sham pooled on pre-specified visual functional measures at 24 months.

## **ABOUT GALE**

GALE (n=792) is a Phase 3, multicenter, open-label, extension study to evaluate the long-term efficacy and safety of SYFOVRE in patients with geographic atrophy (GA). Open-label studies can allow for selection bias. Treatment effect from months 24-48 is compared to a projected sham (rather than an actual sham) that assumes a linear growth rate. This is a prespecified analysis but there is no statistical testing hierarchy. In all GA patients regardless of lesion location, SYFOVRE reduced GA growth by 24% monthly and 23% every other month over 48 months. SYFOVRE reduced GA growth vs. sham by 19% monthly and 18% every other month between months 0 and 24 and reduced GA growth vs. projected sham by 28% monthly and 28% every other month between months 24 and 48 (all  $p < 0.001$ ; nominal). The safety profile in the first 24 months of GALE is consistent with OAKS and DERBY.

In a post hoc analysis at Month 48, the mean area of retinal tissue preserved in patients with NSF GA was 3.16 mm<sup>2</sup> with SYFOVRE monthly and 2.7 mm<sup>2</sup> with SYFOVRE every other month (vs. projected sham).

## **INDICATION**

SYFOVRE® (pegcetacoplan injection) is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

## **IMPORTANT SAFETY INFORMATION**

### **CONTRAINDICATIONS**

SYFOVRE is contraindicated in patients with ocular or periocular infections, in patients with active intraocular inflammation, and in patients with hypersensitivity to pegcetacoplan or any of the excipients in SYFOVRE. Systemic hypersensitivity reactions (e.g., anaphylaxis, rash, urticaria) have occurred.

### **WARNINGS AND PRECAUTIONS**

- **Endophthalmitis and Retinal Detachments**
  - Intravitreal injections, including those with SYFOVRE, may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering SYFOVRE to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.
- **Retinal Vasculitis and/or Retinal Vascular Occlusion**

- Retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intraocular inflammation, have been reported with the use of SYFOVRE. Cases may occur with the first dose of SYFOVRE and may result in severe vision loss. Discontinue treatment with SYFOVRE in patients who develop these events. Patients should be instructed to report any change in vision without delay.
- **Neovascular AMD**
  - In clinical trials, use of SYFOVRE was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (12% when administered monthly, 7% when administered every other month and 3% in the control group) by Month 24. Patients receiving SYFOVRE should be monitored for signs of neovascular AMD. In case anti-Vascular Endothelial Growth Factor (anti-VEGF) is required, it should be given separately from SYFOVRE administration.
- **Intraocular Inflammation**
  - In clinical trials, use of SYFOVRE was associated with episodes of intraocular inflammation including: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, and anterior chamber flare. After inflammation resolves, patients may resume treatment with SYFOVRE.
- **Increased Intraocular Pressure**
  - Acute increase in IOP may occur within minutes of any intravitreal injection, including with SYFOVRE. Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

## ADVERSE REACTIONS

- Most common adverse reactions (incidence  $\geq 5\%$ ) are ocular discomfort, neovascular age-related macular degeneration, vitreous floaters, conjunctival hemorrhage.

Please see full [Prescribing Information](#) for more information.

Sincerely,

Caroline Bauml  
Chief Medical Officer

1. Data on file as of December 31, 2024, including real world and clinical trial injections.
2. Injections are calculated based on 1) vials distributed to eyecare professional (ECP) practices and 2) estimates of patient numbers extrapolated from licensed data and inventory levels from key accounts, representative of our market.