



# TARGETED C3 THERAPIES

November 19, 2020

# Forward-looking Statements

Statements in this presentation about future expectations, plans and prospects, as well as any other statements regarding matters that are not historical facts, may constitute “forward-looking statements” within the meaning of The Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements relating to the implications of preliminary clinical data. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: whether the company’s clinical trials will be fully enrolled and completed when anticipated; whether preliminary or interim results from a clinical trial will be predictive of the final results of the trial; whether results obtained in preclinical studies

and clinical trials will be indicative of results that will be generated in future clinical trials; whether pegcetacoplan will successfully advance through the clinical trial process on a timely basis, or at all; whether the results of the company’s clinical trials will warrant regulatory submissions and whether pegcetacoplan will receive approval from the FDA or equivalent foreign regulatory agencies for GA, PNH, CAD, HSCT-TMA, C3G, IC-MPGN, ALS or any other indication when expected or at all; whether, if Apellis’ products receive approval, they will be successfully distributed and marketed; and other factors discussed in the “Risk Factors” section of Apellis’ Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 2, 2020 and the risks described in other filings that Apellis may make with the Securities and Exchange Commission. Any forward-looking statements contained in this press release speak only as of the date hereof, and Apellis specifically disclaims any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise.

# Targeting C3: Broad Platform Potential with Pegcetacoplan

## **PNH Approval and Launch**

PDUFA is May 14, 2021



*Lani, living with PNH*

## **GA Phase 3 Read-out**

expected in Q3 2021



*Carolyn, living with GA*

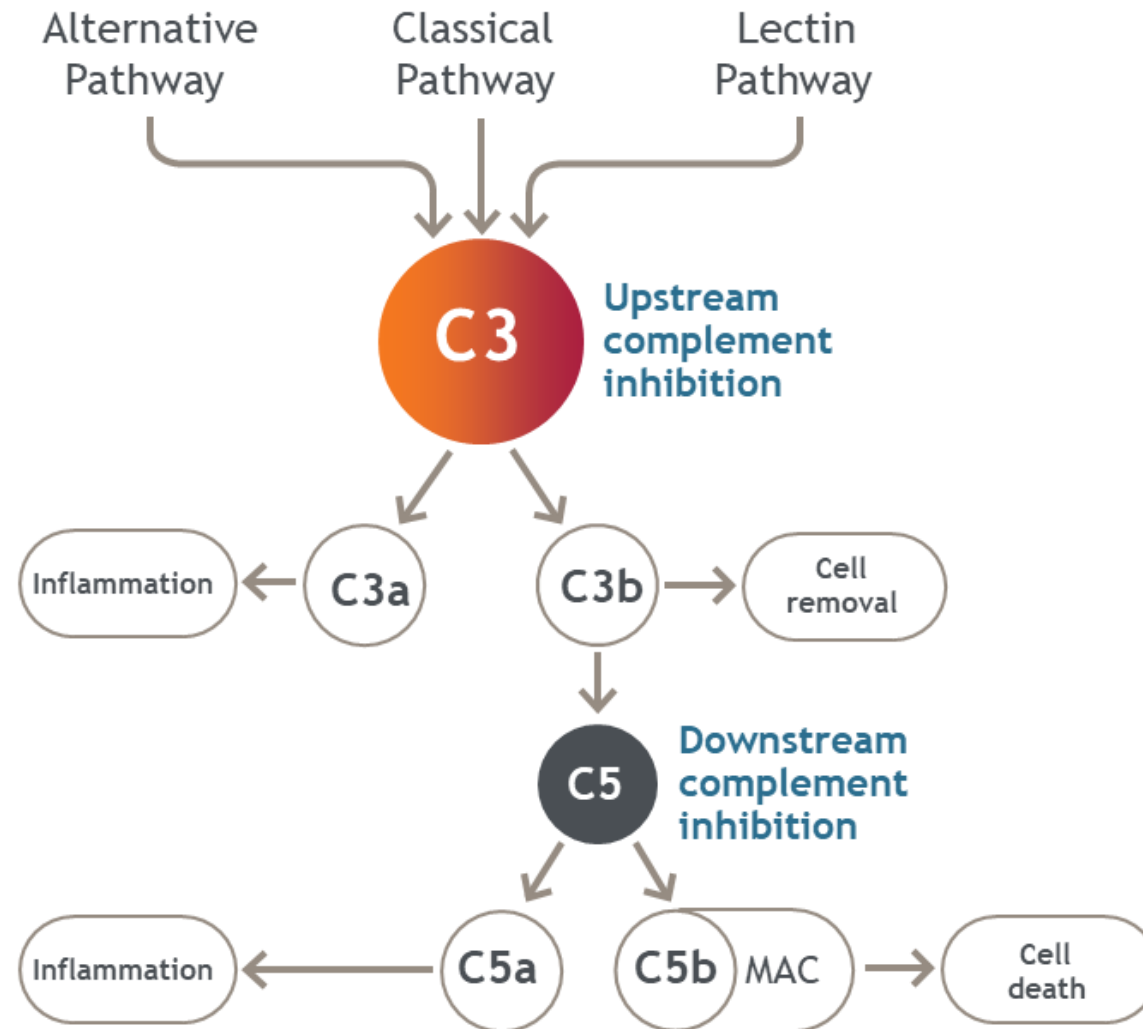
## **4 New Registrational Programs**

across hematology, nephrology  
and neurology



*Bart, living with ALS*

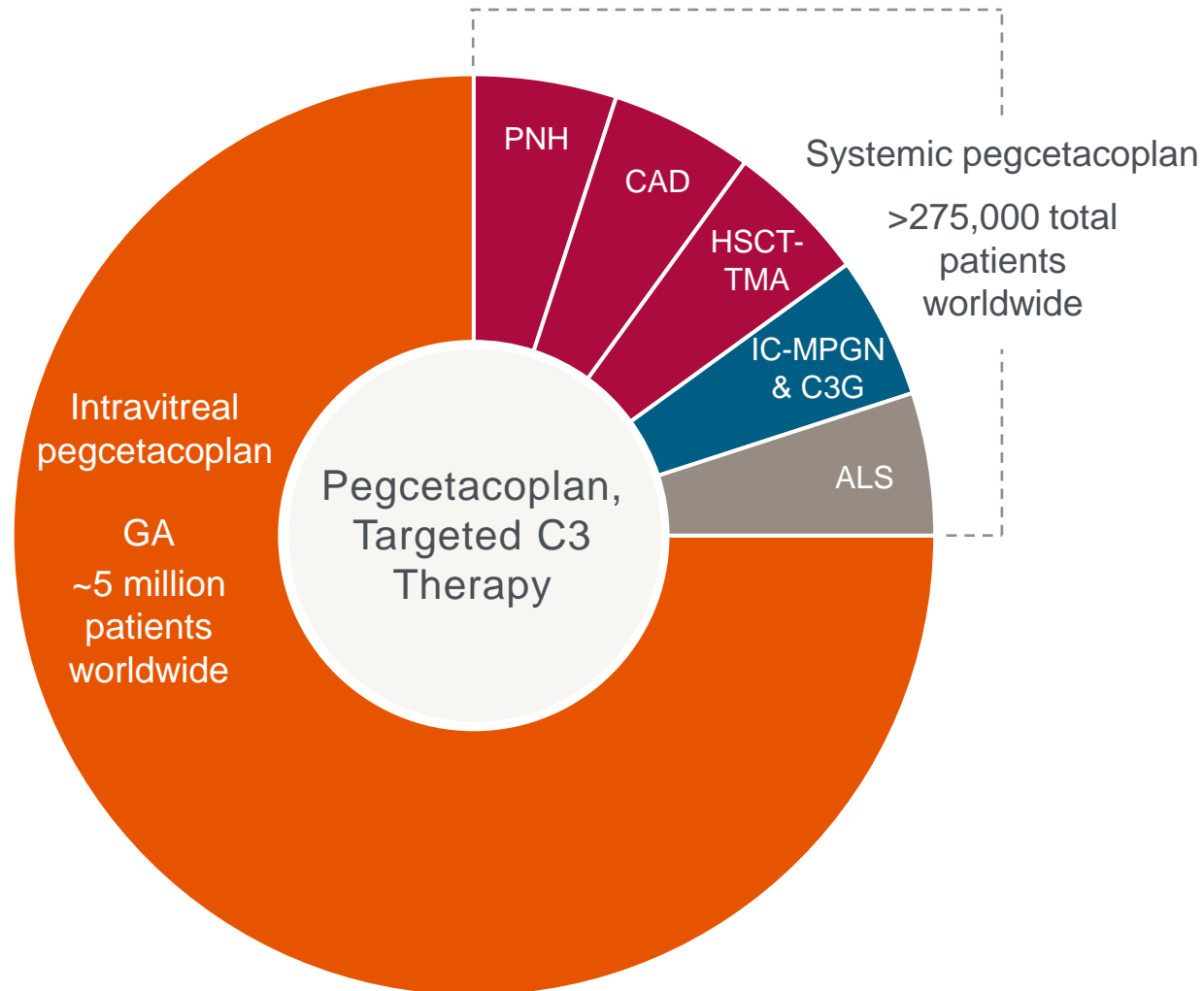
# Targeting C3 to More Completely Control Complement Overactivation



# Targeted C3 Therapies for Diseases with High Unmet Need

Product	Category	Disease	Pre-clinical	Phase 1	Phase 2	Phase 3	Approved
<b>Systemic pegcetacoplan (APL-2)*</b>	Hematology	Paroxysmal nocturnal hemoglobinuria (PNH)					
		Cold agglutinin disease (CAD)					
		Hematopoietic stem cell transplantation thrombotic microangiopathies (HSCT-TMA)					
	Nephrology	Immune complex membranoproliferative glomerulonephritis (IC-MPGN) and C3 glomerulopathy (C3G)					
	Neurology	Amyotrophic lateral sclerosis (ALS)					
<b>Intravitreal pegcetacoplan</b>	Ophthalmology	Geographic atrophy (GA)					
<b>Intravenous APL-9</b>	COVID-19	Acute respiratory distress syndrome (ARDS) & thrombotic microangiopathies (TMA) secondary to COVID-19					
	Gene therapy	Control of host attack on AAVs for gene therapies					

# Sobi Collaboration Advances Pipeline-in-a-Product Opportunity for Systemic Pegcetacoplan



Up to **\$1.25 billion** in payments plus tiered double-digit royalties

## SYSTEMIC PEGCETACOPLAN

Apellis (U.S.)

sobi (ex U.S. and global co-development)  
rare strength

Hematology  
Nephrology  
Neurology

## INTRAVITREAL PEGCETACOPLAN

Apellis (global)

Ophthalmology



Device prototype

## **Systemic Pegcetacoplan:** Preparing for approval and launch in PNH

# PNH Is a Rare and Life-threatening Blood Disease

Estimated prevalence of  
PNH worldwide<sup>1</sup>



**~15,000 patients**

Historically untreated  
patients<sup>2</sup>

**35%**

5-year mortality rate

*Note: Thrombosis and  
hemorrhage are the most  
common causes of death.*




# PNH Patients on C5 Inhibitors Continue to Have High Unmet Need


Retrospective studies show:

Up to 70% 

of patients continue to have low hemoglobin despite treatment<sup>1,2,3</sup>

36% 

of patients require  $\geq 1$  transfusion per year<sup>3,4</sup>

100% 

of patients on eculizumab had evidence of C3-opsonized PNH RBCs<sup>1</sup>

1.9x ULN 

average absolute reticulocyte count<sup>3</sup>

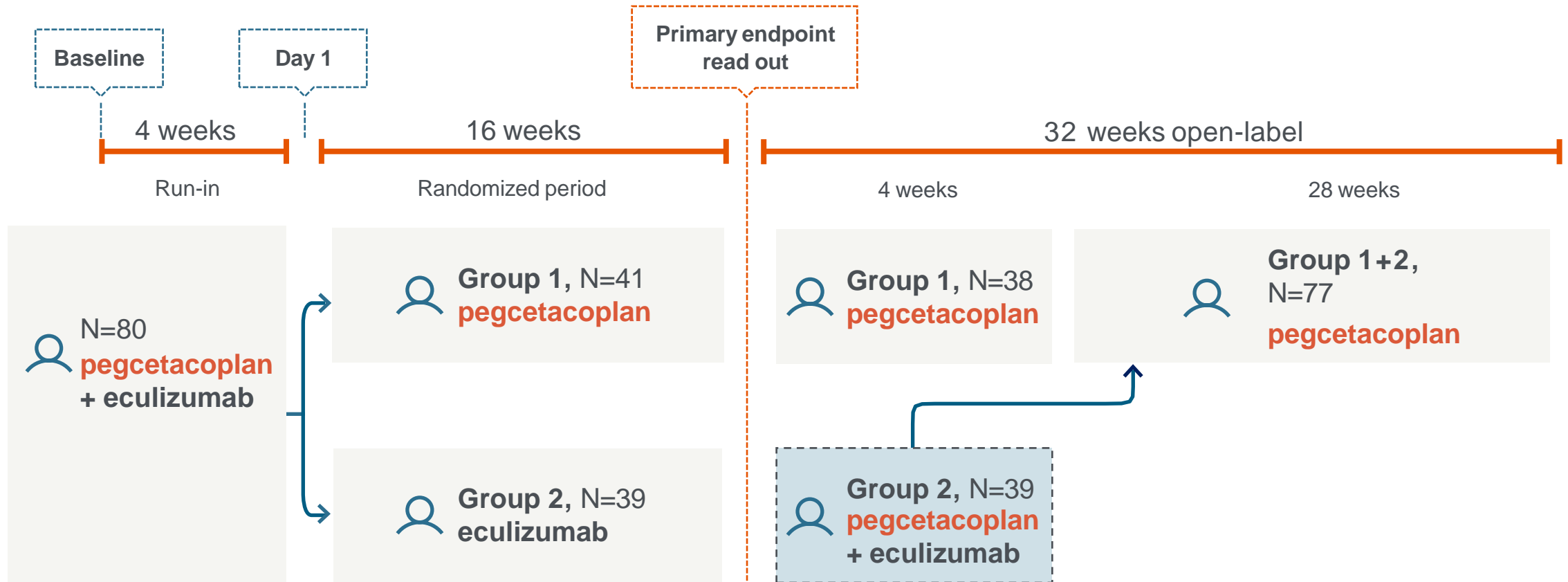
1 Risitano AM, Marotta S, Ricci P, et al. (2019) Anti-complement Treatment for Paroxysmal Nocturnal Hemoglobinuria: Time for Proximal Complement Inhibition? A Position Paper From the SAAWP of the EBMT. Front. Immunol. 10:1157. doi: 10.3389/fimmu.2019.01157.

2 Risitano AM, Notaro R, Marando L, et al. (2009) Complement fraction 3 binding on erythrocytes as additional mechanism of disease in paroxysmal nocturnal hemoglobinuria patients treated by eculizumab. Blood. 2009 Apr 23;113(17):4094-100.

3 Dingli D. et al. Clinical Burden of Paroxysmal Nocturnal Hemoglobinuria Among Patients Receiving C5 Inhibitors in the United States. Blood 2020; 136 (Supplement 1): 2.

4 McKinley C. Extravascular Hemolysis Due to C3-Loading in Patients with PNH Treated with Eculizumab: Defining the Clinical Syndrome. Blood. 2017;130:3471

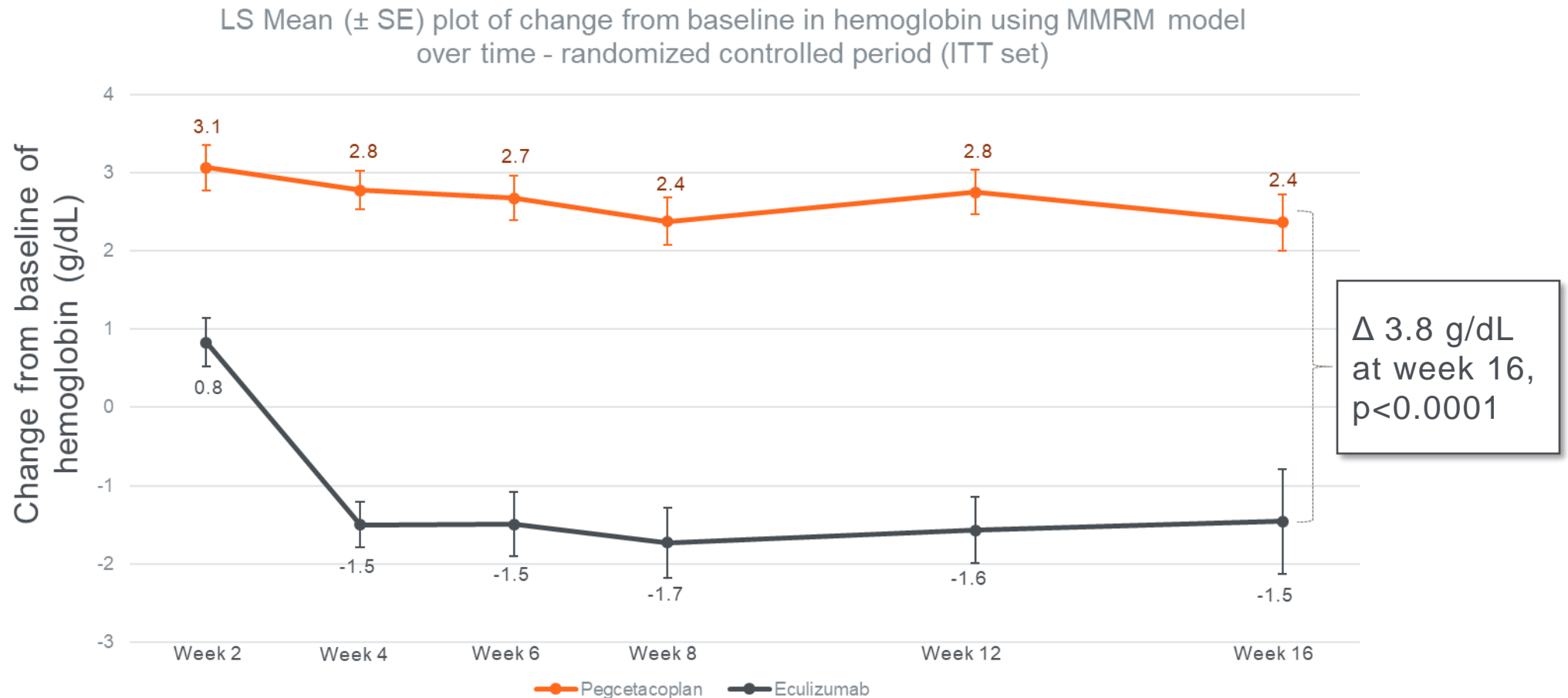
# PEGASUS: Phase 3 Head-to-head Trial of Pegcetacoplan vs Eculizumab



APL2-302; NCT03500549

# Pegcetacoplan Met its Primary Endpoint in Phase 3 PEGASUS Study (MMRM)

**3.8 g/dL improvement in adjusted means in hemoglobin vs. eculizumab at week 16,  $p < 0.0001$**



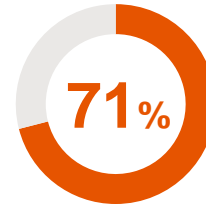
# Pegcetacoplan Demonstrated Substantial Improvement over C5 Inhibitor at Week 16

TARGETED C3 THERAPY PEGCETACOPLAN VS. C5 INHIBITOR ECULIZUMAB

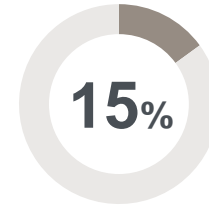
**45%**  
HIGHER



**hemoglobin levels**  
pegcetacoplan  
over eculizumab



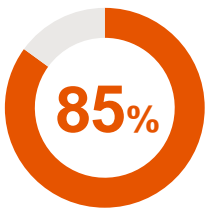
**VS.**



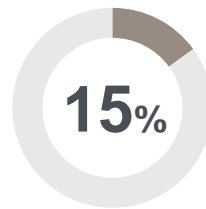
PEGCETACOPLAN

ECULIZUMAB

Patients with **normalized LDH**



**VS.**



PEGCETACOPLAN

ECULIZUMAB

Patients were **transfusion-free**



**11-point difference**

**FACIT-fatigue score** in patients with  
pegcetacoplan over eculizumab

# Safety Profile of Pegcetacoplan Was Comparable to Eculizumab at Week 16 in PEGASUS Study

---

- Seven of 41 patients (17%) in the pegcetacoplan group experienced a serious adverse event (SAE) and six of the 39 patients (15%) in the eculizumab group experienced SAEs
- No cases of meningitis and no deaths were reported in either treatment group

# Prepared to Meet the Needs of PNH Patients

## Our Goal: Elevate the Standard of Care in PNH

**U.S. MEDICAL &  
COMMERCIAL  
ORGANIZATION**

Highly Experienced  
Team



*Lani, living with PNH*

**PATIENT FOCUSED**

Support and Access  
for Patients



*Carolyn, living with GA*

## **Intravitreal Pegcetacoplan:** **Delivering the first potential treatment in geographic atrophy**

# High Unmet Need in Geographic Atrophy (GA)

**5M**  
**PATIENTS**  
**GLOBALLY**  
**NO APPROVED**  
**THERAPIES**



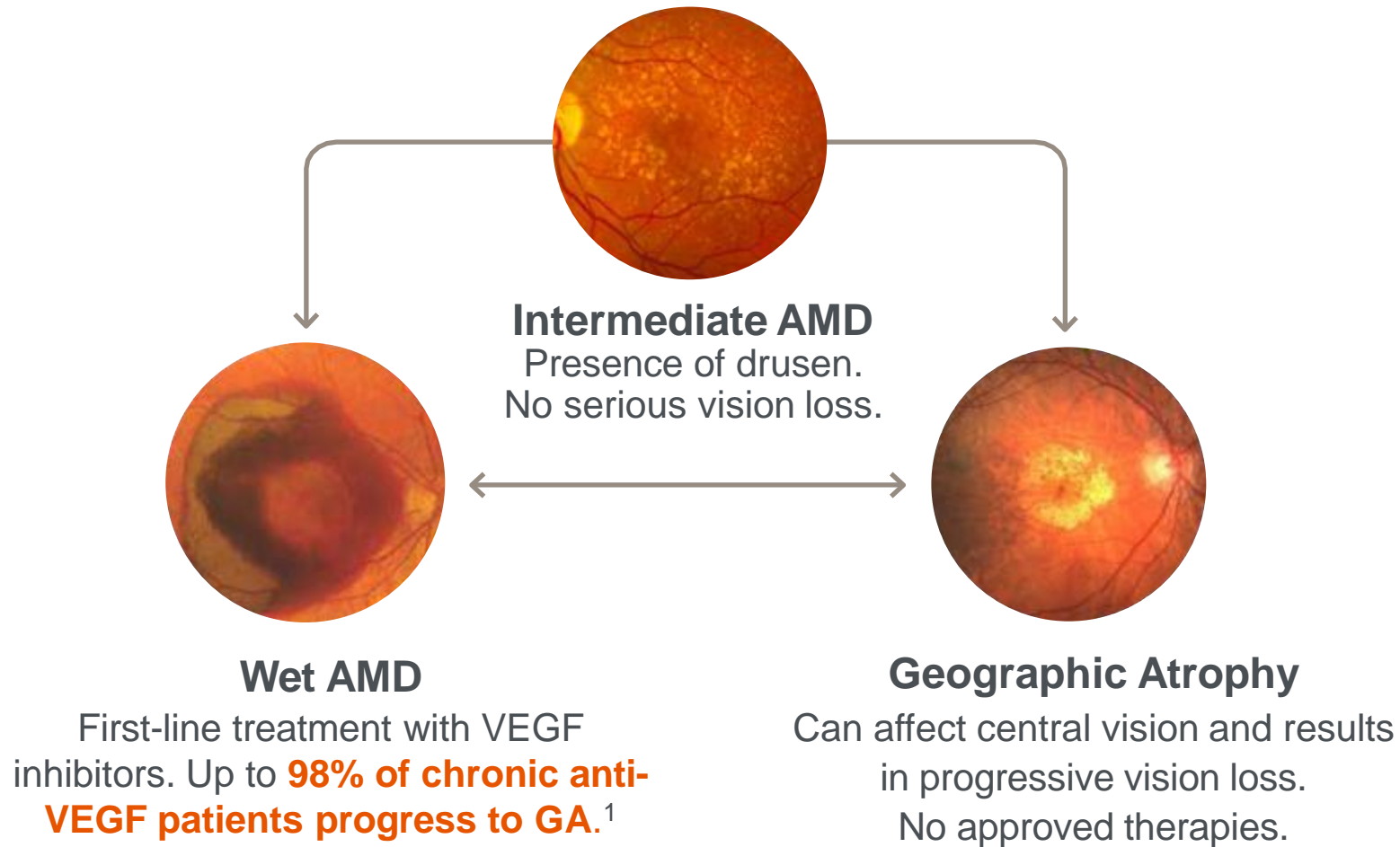
Normal vision



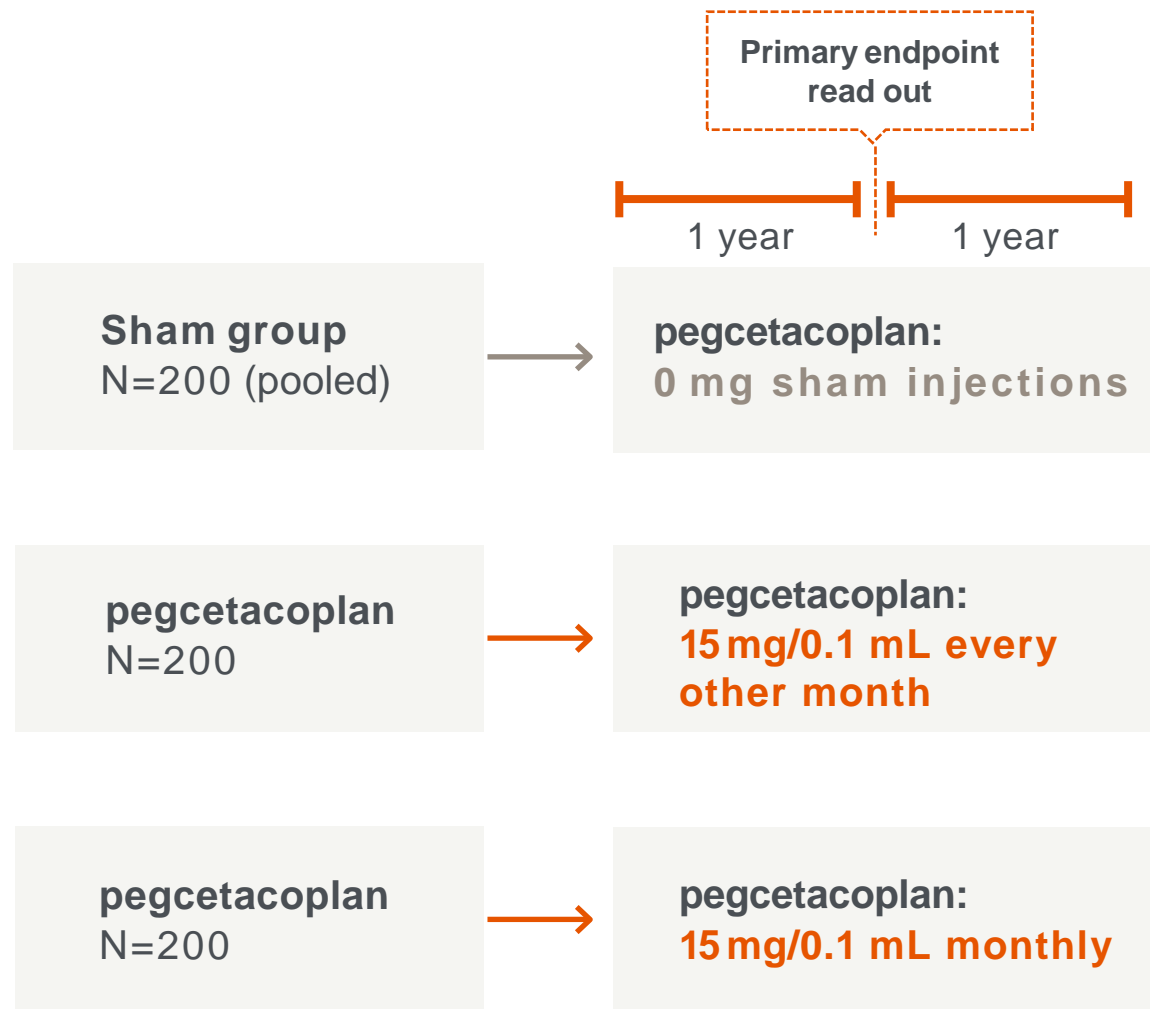
Vision with advanced GA



# GA: Advanced Form of Age-related Macular Degeneration (AMD)



# DERBY & OAKS: Two Phase 3 Studies Enrolled (n=1,256) with Top-Line Data Expected in Q3 2021



**Population:** patients with Geographic Atrophy secondary to AMD

**Primary endpoint:** change in total area of GA lesion(s) based on Fundus Autofluorescence (FAF) at month 12

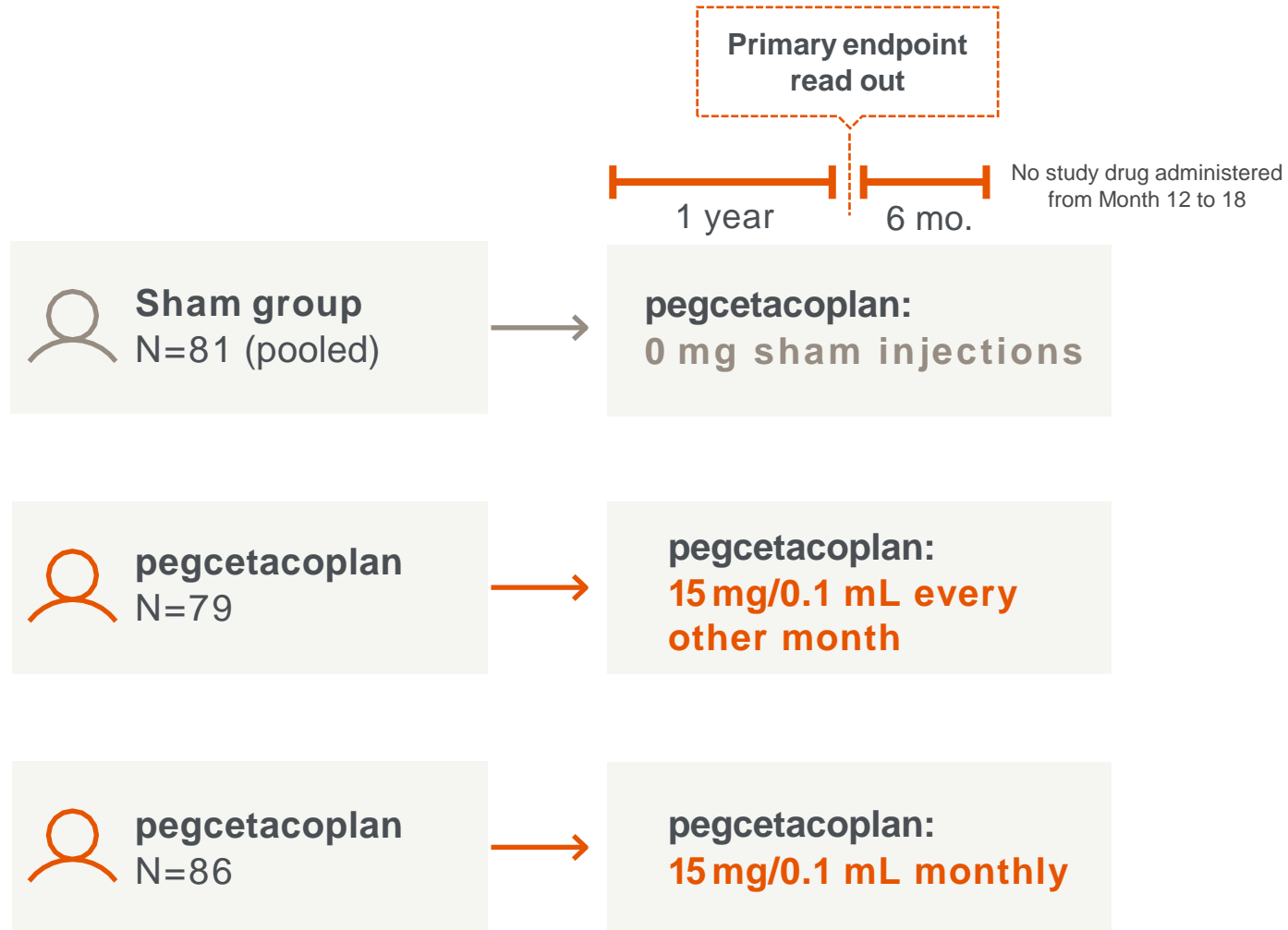
**Design:** doublemasked, randomized 2:1:2:1

**Treatment:** 15 mg/0.1 mL intravitreal injection vs. Sham injection.

**Sample size:** >600 subjects from approx. 100 multinational sites per study

**Duration:** 2 years

# Phase 2 FILLY Study: Design



**Population:** patients with geographic atrophy\* secondary to AMD

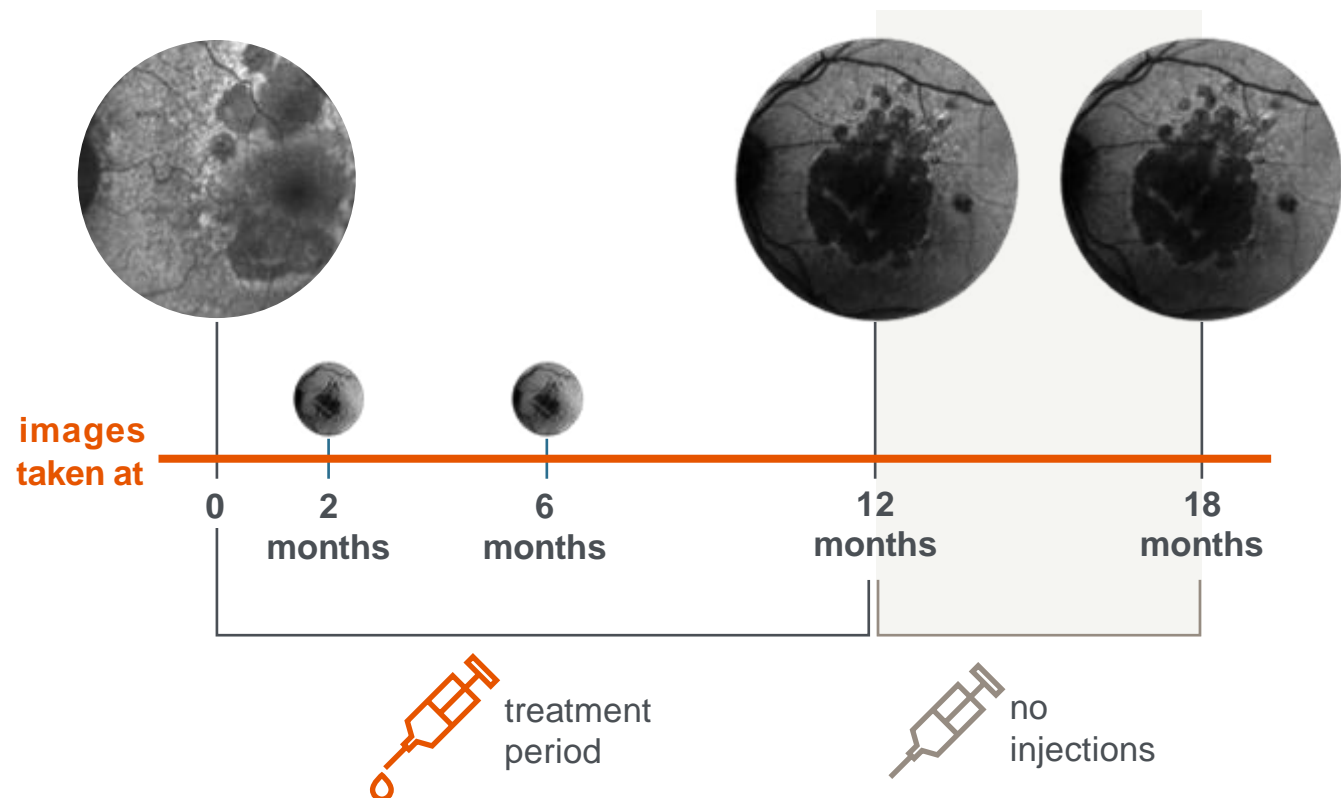
**Design:** single masked, randomized 2:1:2:1

**Treatment:** 15 mg/0.1 mL intravitreal injection vs. sham injection

**Sample size:** 246 subjects at 46 sites<sup>#</sup>

**Duration:** 18 months

# Phase 2 FILLY Study: Timeline and Endpoints



## Primary efficacy endpoint

Change in geographic atrophy (GA) lesion size from baseline at month 12

## Primary safety endpoint

Number and severity of local and systemic treatment emergent adverse events (TEAEs)

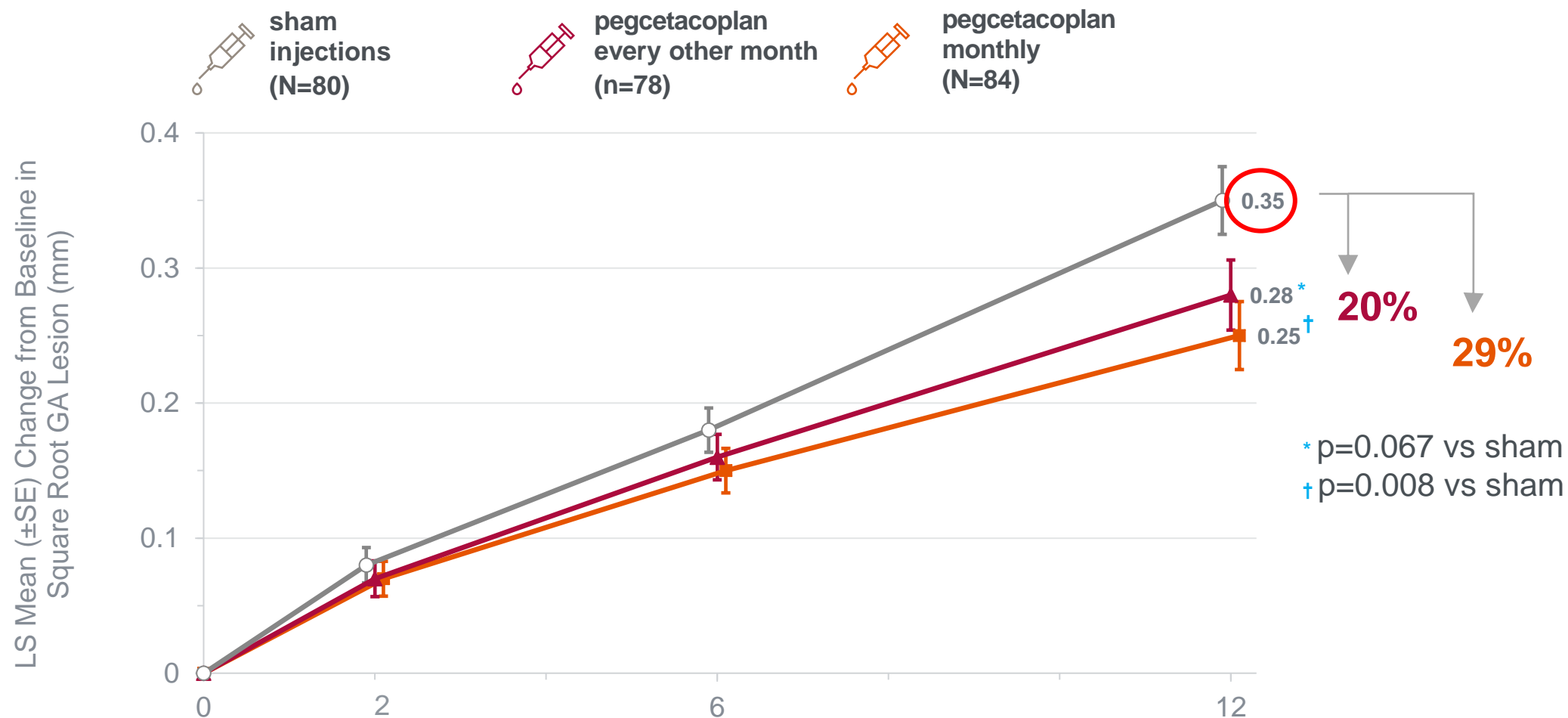
# FILLY Study: Pegcetacoplan Reduced GA Lesion Growth

- ✓ Dose response
- ✓ Increased effect over time
- ✓ Effect in treated versus contralateral non-treated eye
- ✓ Sham group as expected
- ✓ **Modeled data consistent with observed data**

**26 FILLY subjects (11%) had exudations** (18 monthly, 7 every-other-month, 1 sham)

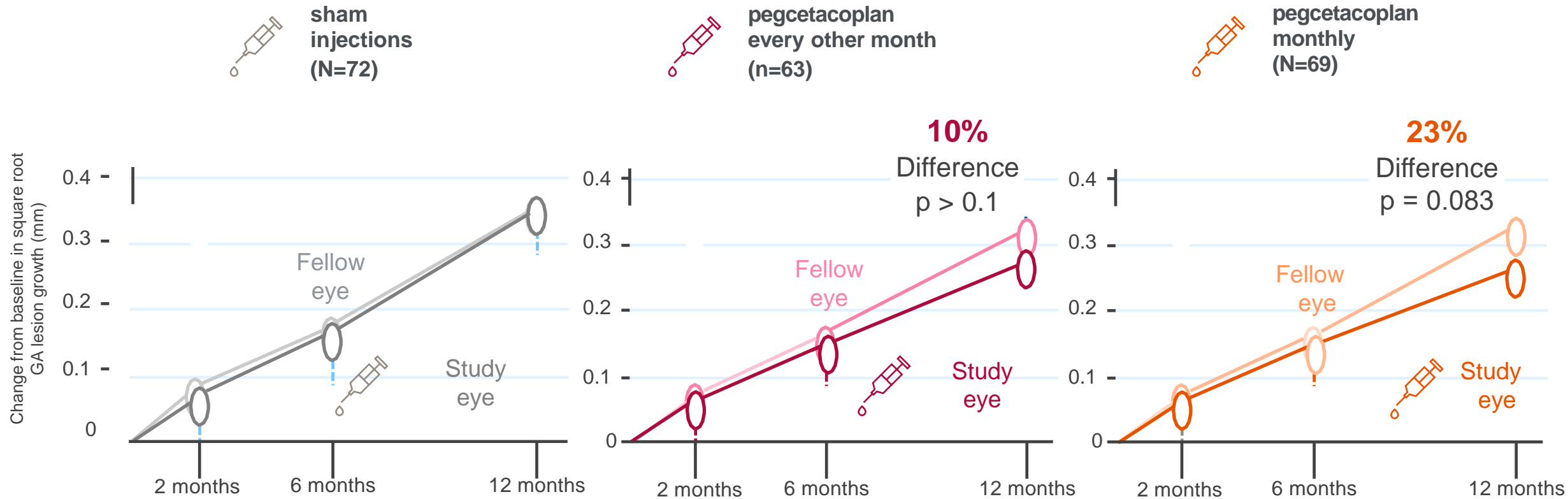
- **0 cases of classical CNV**
- No impact on vision
- Safety was in line with other studies using intravitreal administration

# Phase 2 FILLY: Pegcetacoplan Reduced GA Growth at 12 Months



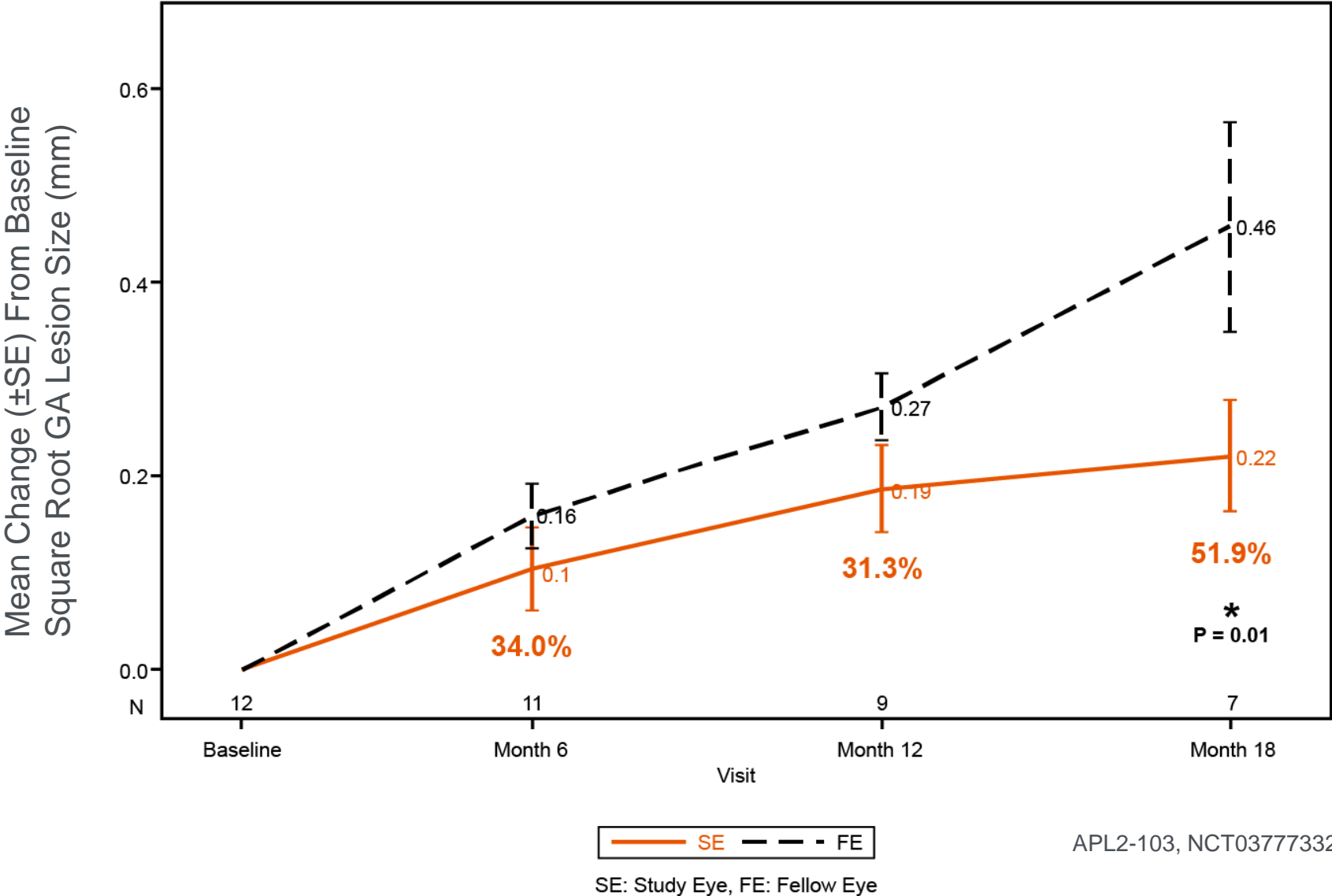
Change from baseline in square root of GA area at 48 wk, mm	Sham	Lampalizumab, 10mg <sup>1</sup>	
	Pooled (n=598)	Q4w (n=596)	Q6w (n=603)
Adjusted mean (SE)	0.342 (0.007)	0.349 (0.007)	0.352 (0.007)

# Pegcetacoplan Decreased Lesion Growth in Treated Eye vs. Untreated Fellow Eye in FILLY Post Hoc Analysis



Includes patients from the Bilateral GA Population

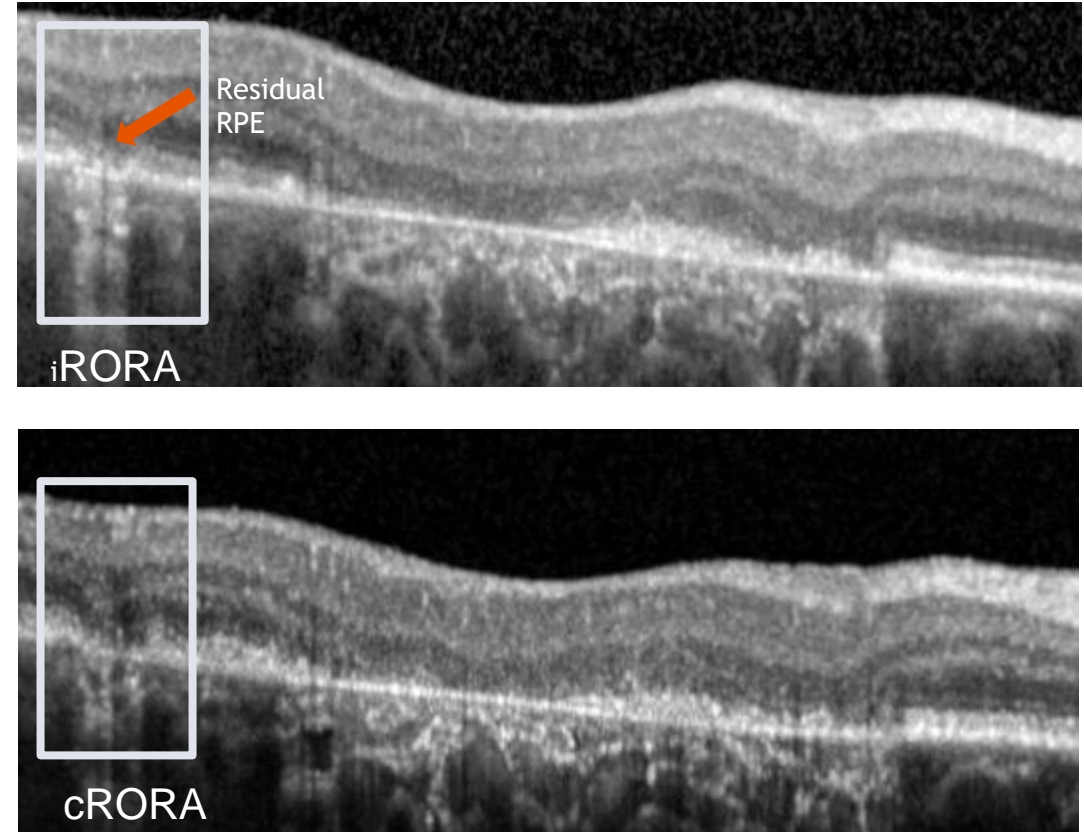
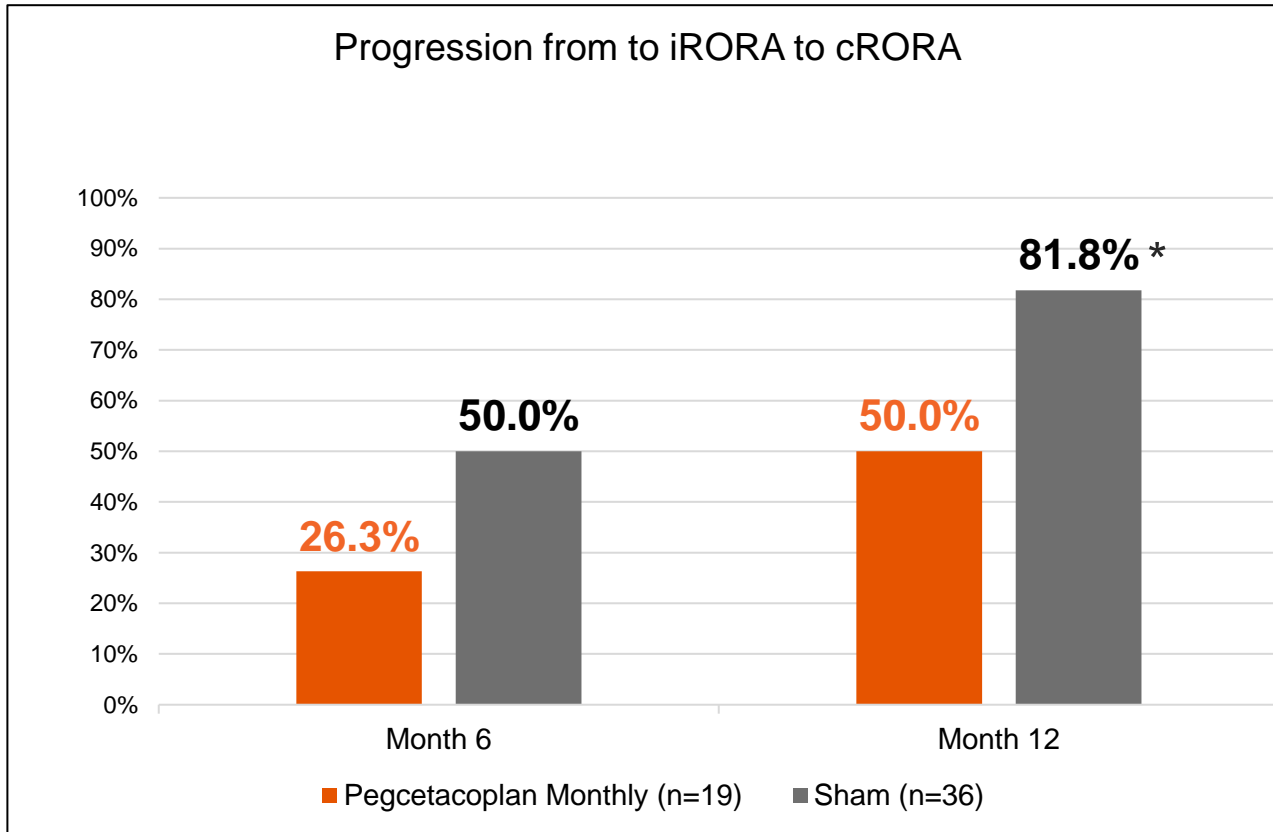
# Pegcetacoplan Decreased Mean Lesion Growth 52% in 7 Patients with Bilateral GA in Phase 1b Post Hoc Analysis





# Pegcetacoplan Slowed Progression of Early Disease in GA Patients in FILLY Post Hoc Analysis

GA



Pearson Chi-Square:  
Month 6 -  $P=0.08$ ; \*Month 12 -  $P=0.02$   
Relative risk:  
Month 12 - 0.61 (0.37- 1.00)



**Expanded Pipeline:**  
**Advancing 4 rare disease  
registrational programs**

# Initiated Registrational Programs of Systemic Pegcetacoplan in Nephrology and Neurology

## Immune Complex Membranoproliferative Glomerulonephritis (IC-MPGN) & C3 Glomerulopathy (C3G)



**Current Treatments:** No approved therapies

**Market Opportunity:** ~18,000 patients in US and Europe<sup>1</sup>

### Next Steps:

- First patient dosed by end of the year in Phase 2 trial focused on histopathology of the kidney
- First patient dosed in Phase 3 study in 1H21 (Apellis)

## Amyotrophic Lateral Sclerosis (ALS)



**Current Treatments:** No approved therapies have been shown to stop or reverse disease progression

**Market Opportunity:** ~225,000 patients worldwide<sup>2</sup>

### Next Steps:

- ✓ First patient dosed in potentially registrational Phase 2 study by end of 2020 (Apellis)

# Plan to Start Two New Registrational Programs of Systemic Pegcetacoplan in Hematology in 2021



## Cold Agglutinin Disease (CAD)

**Current Treatments:** No approved therapies

**Market Opportunity:** ~10,500 patients in US and Europe<sup>1</sup>

### Next Steps:

- Initiate Phase 3 trial in 2021 (Sobi)



## Hematopoietic Stem Cell Transplantation (HSCT)–associated Thrombotic Microangiopathy (TMA)

**Current Treatments:** No approved therapies

**Market Opportunity:** ~9,000 and ~18,000 allogeneic transplants conducted in U.S. and EU+ annually.<sup>2,3</sup> TMA incidence can be up to 40%<sup>4</sup>

### Next Steps:

- Initiate potentially registrational Phase 2 study in 2021 (Sobi)

# Unlocking the Broad Potential of Targeting C3

## PNH

- 48-week top-line PEGASUS data by end of 2020
- PDUFA May 14, 2021
- Phase 3 PRINCE top-line H1 2021
- EU CHMP opinion 2021

## Geographic Atrophy

- Phase 3 DERBY & OAKS read-out Q3 2021

## Pipeline

- ✓ Initiated registrational programs in nephrology (IC-MPGN/C3G) and neurology (ALS)
- Start two registrational programs in hematology (CAD and HSCT-TMA) in 2021
- Progress APL-9 in COVID-19





# TARGETED C3 THERAPIES

November 19, 2020