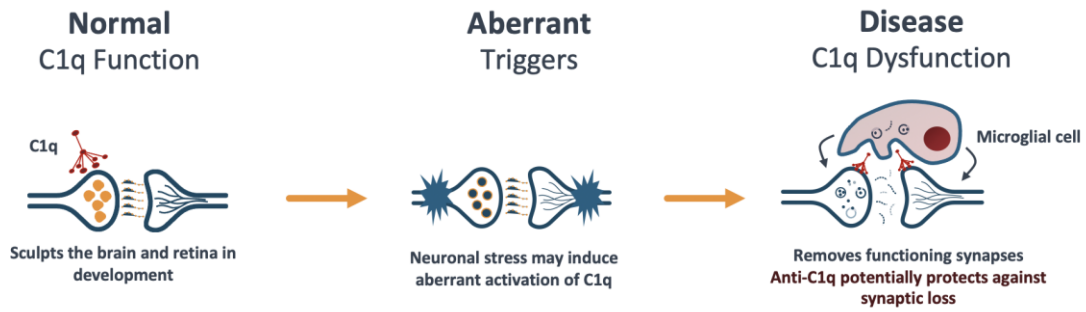
Inhibition of C1q Protects Photoreceptor Synapses in a Light Damage Model and is a Potential Treatment for Geographic Atrophy

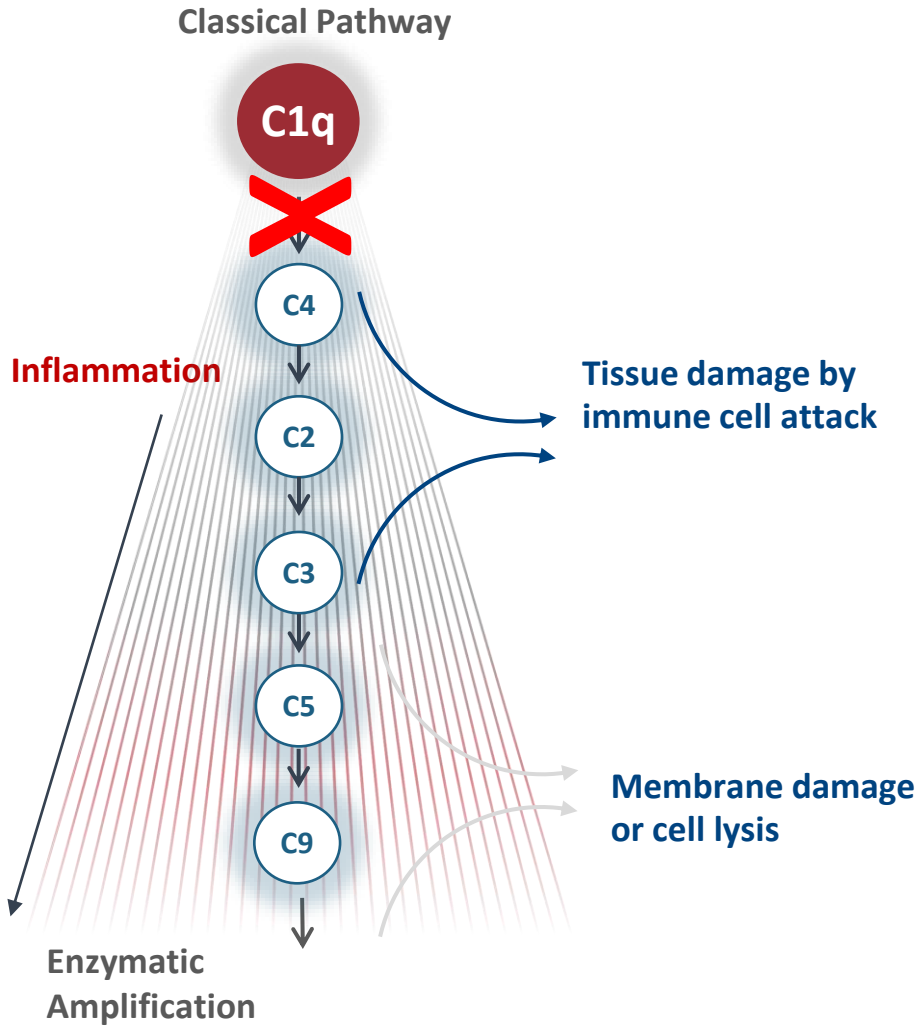
Roger Goldberg, MD

Joseph Vereen, Yaisa Andrews-Zwilling, Ellen Cahir-McFarland, Larry Mattheakis, Ted Yednock, and Alessia Tassoni

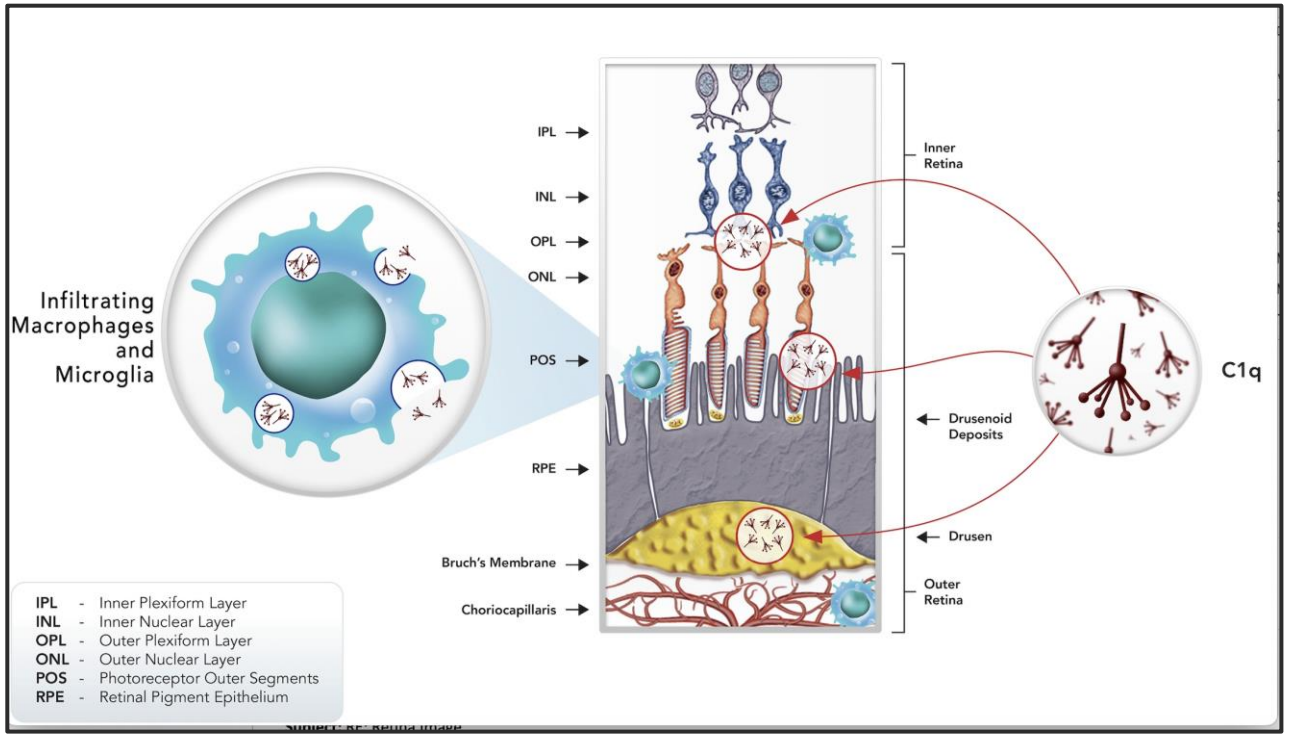
ANX007 Stops Complement Pathway at the Start

- Blocks all downstream components of the classical complement pathway
- Preserves normal immune function of the lectin and alternative complement pathways
- Provides neuroprotection to stressed photoreceptor cells

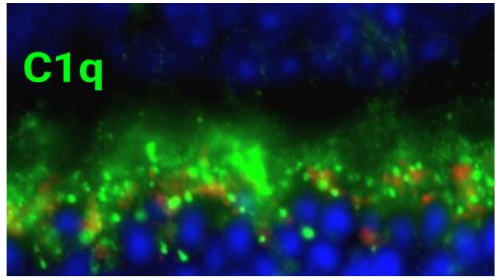




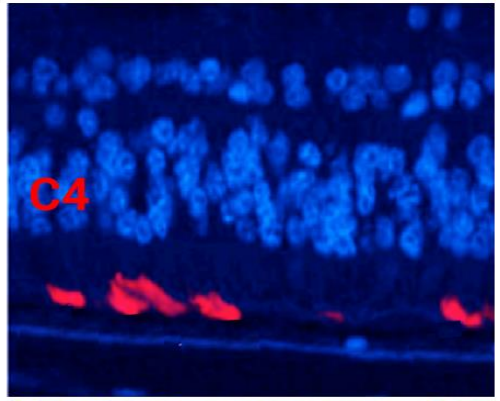
C1q Present throughout Outer Retina



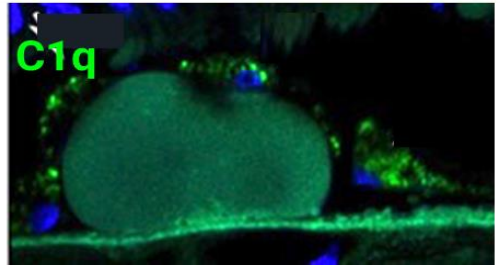
Photoreceptor synapses



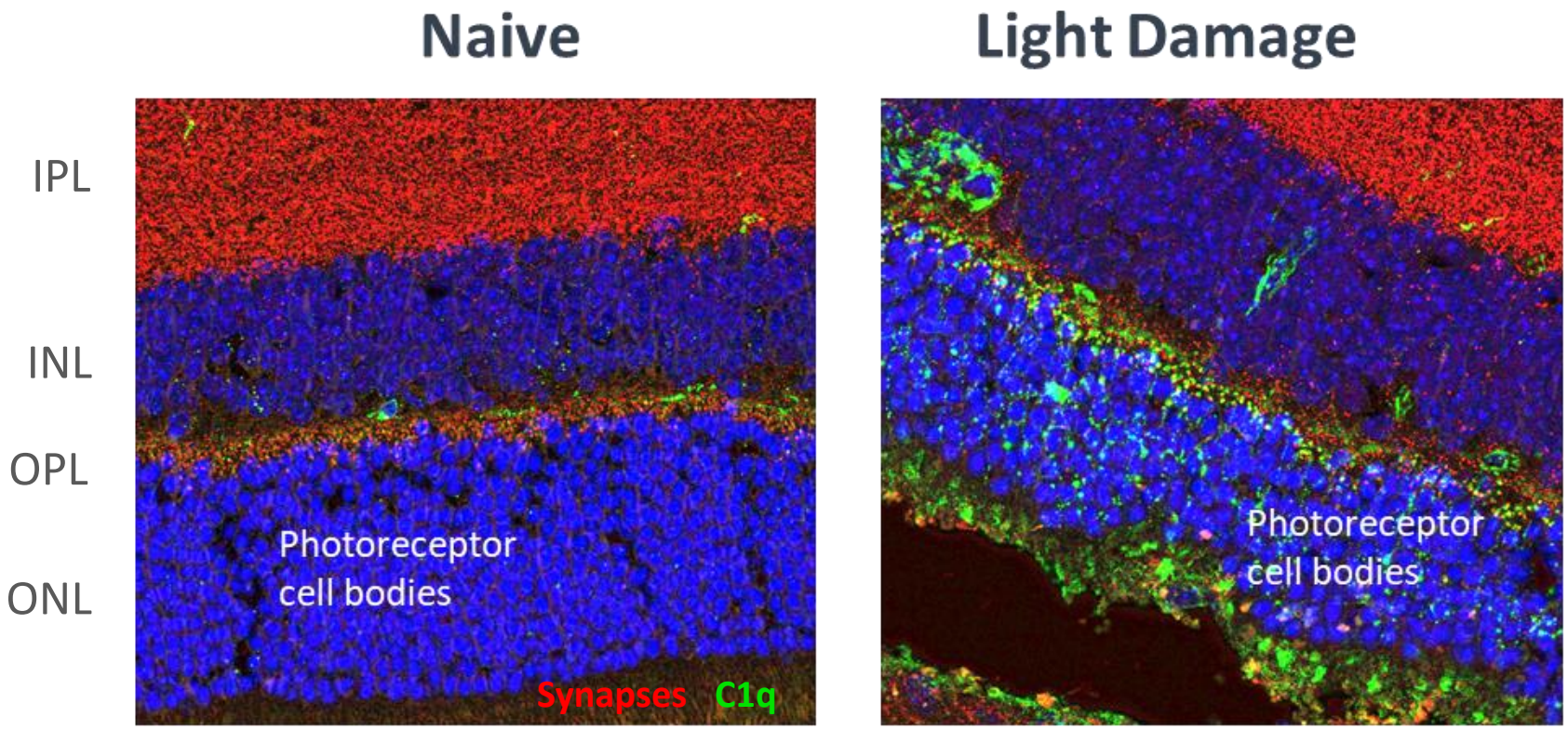
Photoreceptor outer segments



Drusen below photoreceptors



Increased C1q expression at Photoreceptor Cell Bodies

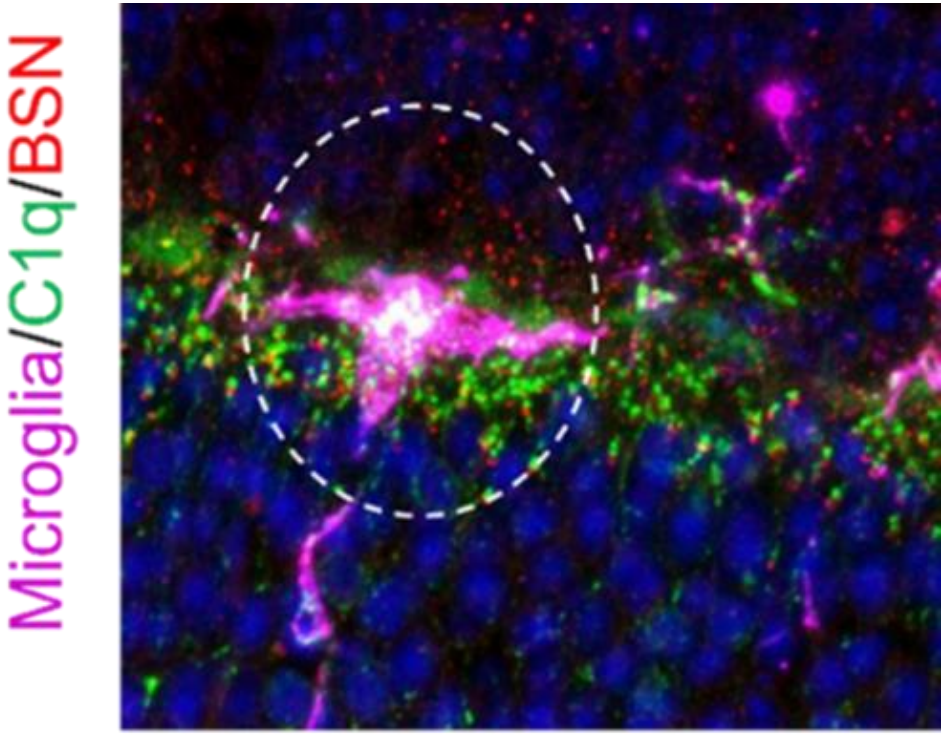


Annexon data on file

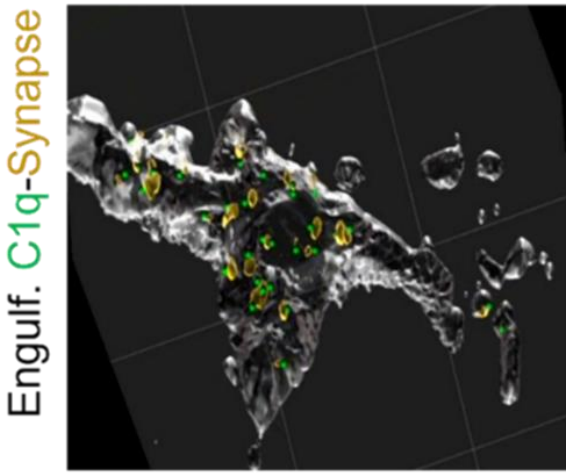
Balb/c mice were exposed to white light to cause retinal damage. C1q activity was pharmacologically blocked by intravitreal injection of a C1q inhibitory antibody (ANX-M1.21) one day prior light exposure. Tissue was assessed at Day 3 and 5 after treatment by ELISA and IHC

Microglial Cell Engulfment of C1q-Tagged Photoreceptor Synapses

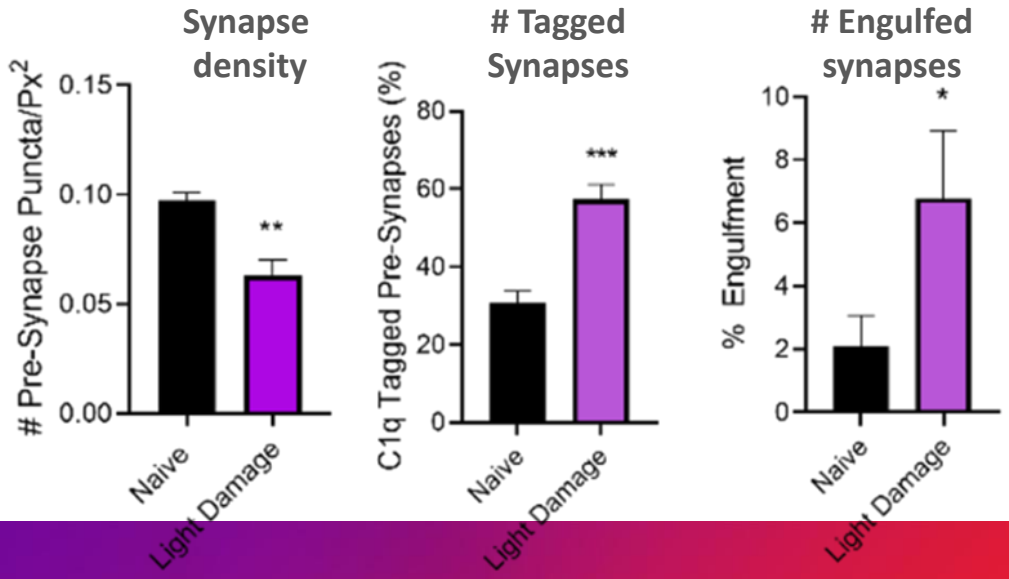
Microglial infiltration of OPL



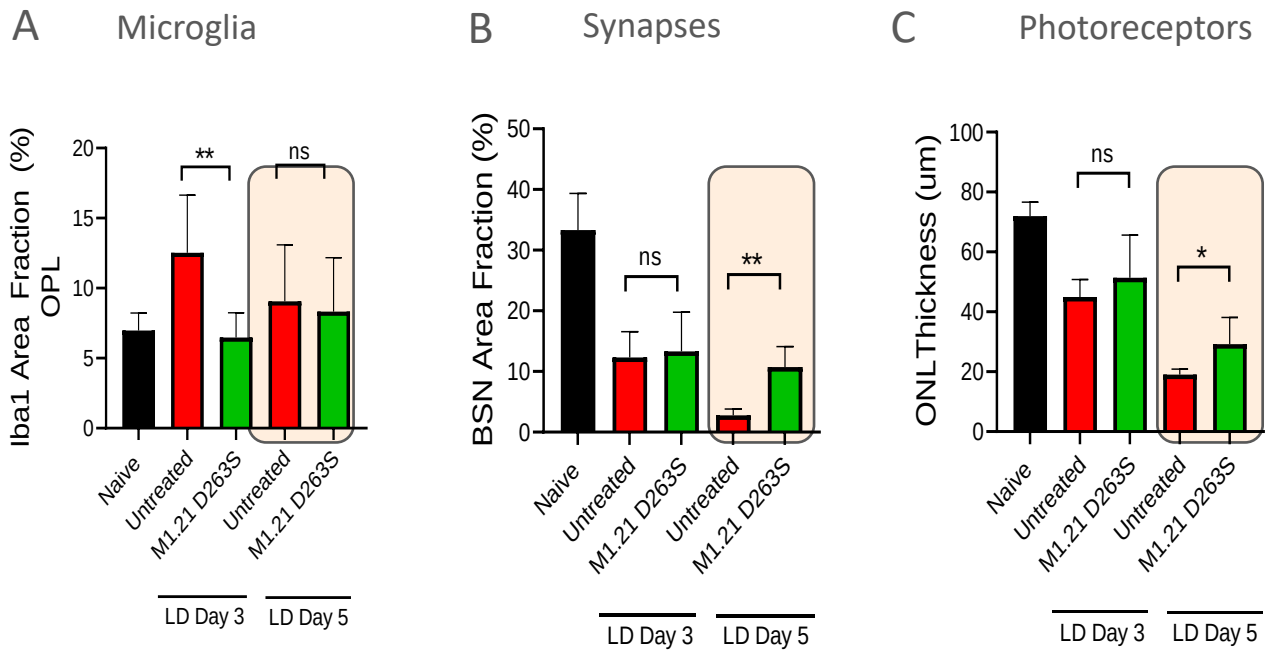
High resolution 3D surface rendering



Microglial cell engulfment of C1q tagged synapses in light damaged retina



Anti-C1q Reduces Neurodegeneration in a Light Damage Model

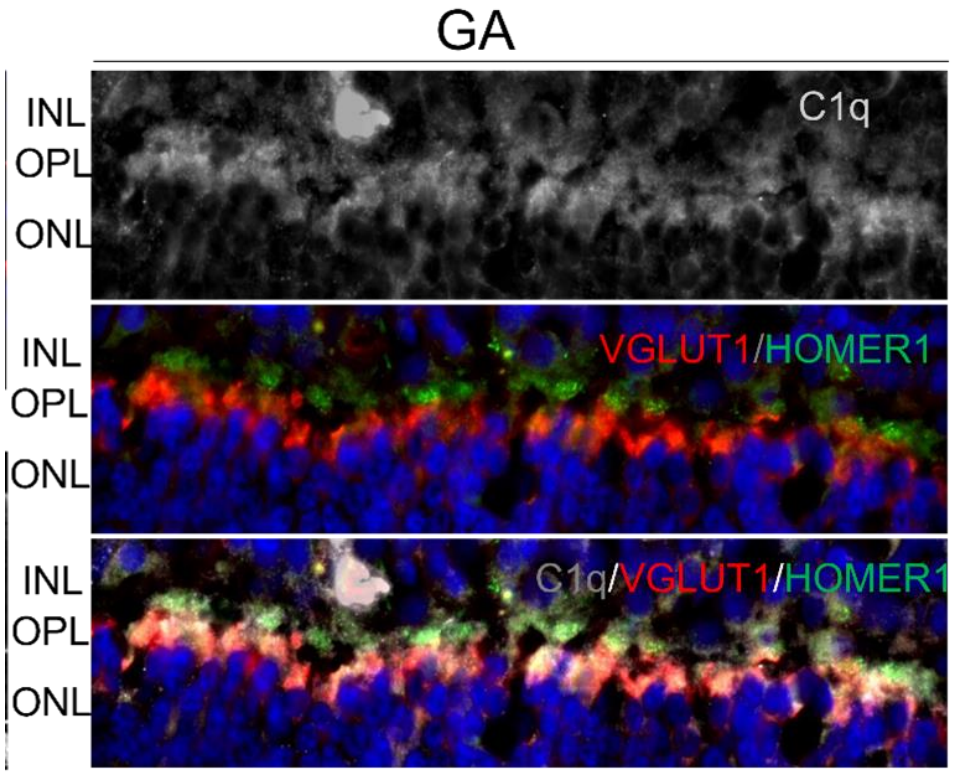


Preliminary immunofluorescence data shows –

- Reduced microgliosis in the OPL at Day 3 post treatment
- Significant preservation of photoreceptor synapses and cell bodies at Day 5 post treatment

Annexon data on file

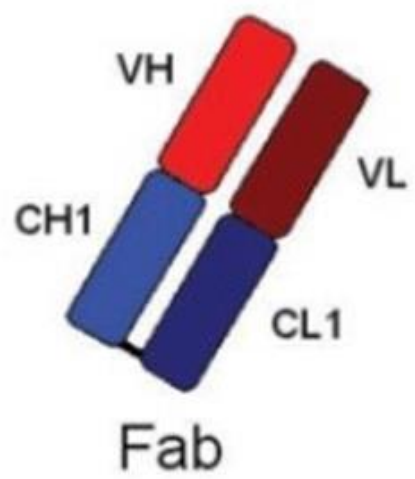
C1q Deposition on Photoreceptor Synapses in Human GA Retina



Triple immunolabelling for C1q (grey), presynaptic marker VGLUT1 (red) and postsynaptic marker (HOMER1) confirming co-localization of C1q with photoreceptor synapses in human GA donor retina

Retina specimens from GA patients were procured from the San Diego Eye Bank

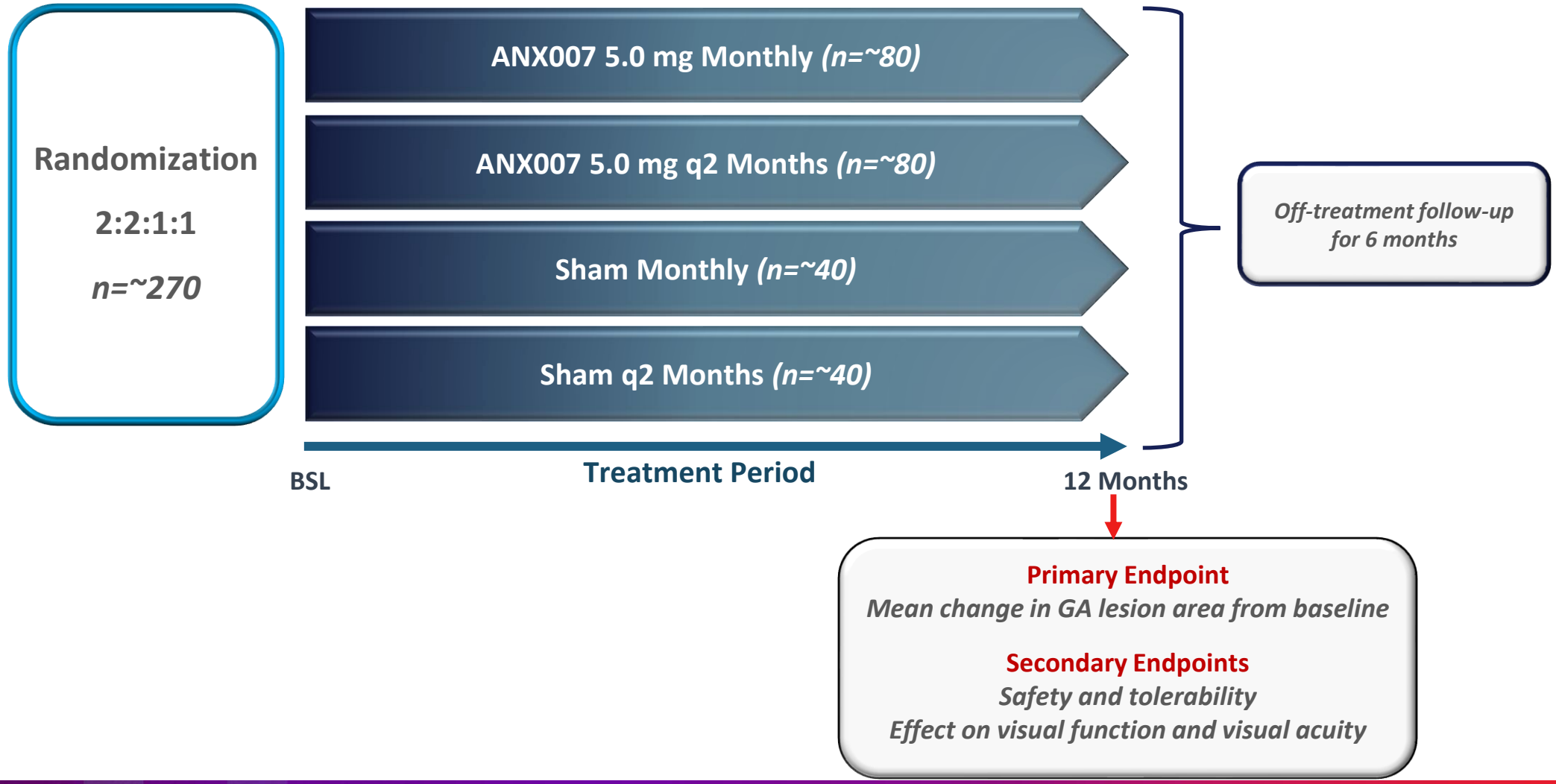
ANX007 is Designed to Inhibit C1q



- Recombinant humanized antigen binding fragment (Fab) of a monoclonal antibody
- Composed of one VH and CH1 segment of an IgG1 heavy chain covalently linked to one kappa light chain
- Molecular weight - ~48 kDa
- Binds to the complement protein C1q via its antigen binding domain

Data on File, Annexon

The ARCHER Study: *Ongoing Phase 2 Study Evaluating Effect of ANX007*



Summary

- Blocking C1q stops classical complement cascade and immune cell phagocytosis **At the Start**
- Anti-C1q treatment is **neuroprotective** in the light damage model
- ANX007 allows normal immune functions of lectin and alternative complement pathways to continue
- ***Enrollment complete for*** ARCHER study evaluating GA lesion growth rate